A PROSPECTIVE OPEN LABELLED RANDOMIZED CLINICAL TRIAL OF "SEENTHIL SARKKARAI" FOR IYA NEERIZHIVU

(CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TYPE II DIABETES MELLITUS)

Dissertation submitted to

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CERTIFICATE

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DECLARATION

I declare that the dissertation entitled "**A Prospective Open Labelled Randomized Clinical Trial of "SEENTHIL SARKKARAI" for IYA NEERIZHIVU** (CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TYPE II DIABETES MELLITUS)" submitted for the degree of MD Siddha Medicine of Government Siddha Medical College, Palayamkottai, Tirunelveli, Tamil Nadu, India. The record of work carried out by me under the guidance of **Dr. S. Justus Antony M.D(S).,** Lecturer (Grade II) Department of Pothu Maruthuvam, Government Siddha Medical College, Palayamkottai, and under the supervision of **Prof.Dr.A.Manoharan, MD (S), Ph.D.,** Head, Department of Pothu Maruthuvam, Government Siddha Medical College, Palayamkottai. This work has not formed the basis of award of any degree, diploma, associateship, fellowship or other titles in the university or any other university or institution of higher learning.

Signature of the candidate

(Dr. SARANGAPANY UTHAYANAN)

Place : Palayamkottai

Date :

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ABBREVIATIONS

ADA	-	American Diabetes Association
ATP III	-	Adult Treatment Panel III
AMORIS	-	Apo lipoprotein-Related Mortality Risk
ASM	-	Airway smooth muscle
BAI	-	Body Adiposity Index
BMI	-	Body Mass Index
CHD	-	Coronary Heart Disease
CETP	-	Cholesteryl Ester Transfer Protein
CD	-	Cluster of Differentiation
COPD	-	Chronic Obstructive Pulmonary Disease
CVD	-	Cardiovascular Disease
CRP	-	C-reactive protein
DM	-	Diabetic Mellitus
DCCT	-	Diabetes Control and Complication Trial
DLCO	-	Lung diffusing capacity for carbon monoxide
EDIC	-	Epidemiology of Diabetes Intervention and Complication
FEV1	-	Forced expiratory volume in one second
FVC	-	Forced vital capacity
GAD	-	Glutamic-acid-decarboxylase
HBAIC	-	Glycated Haemoglobin
HC	-	Hip Circumference
HDL-C	-	High Density Lipoprotein Cholesterol
HIF	-	Hypoxia inducible factor
HSL	-	Hormone-sensitive Lipase
ICS	-	Inhaled corticosteroid
IDF	-	International Diabetic Federation
IL-6	-	Interleukin 6
IGT	-	Impaired Glucose Tolerance
IDDM	-	Insulin Dependent Diabetes Mellitus
LDL-C	-	Low Density Lipoprotein Cholesterol
LPL	-	Lipoprotein Lipase
MMEF	-	Maximal mid-expiratory flow rate

NIDDM	-	Non-Insulin Dependent Diabetes Mellitus
NHDL-C	-	Non High Density Lipoprotein Cholesterol
NGSP	-	National Glycohaemoglobin Standardisation Programme
NCEP	-	National Cholesterol Education Program
OGTT	-	Oral Glucose Tolerance Test
PDE4	-	Phosphodiesterase 4
PFT	-	Pulmonary Function Test
ROS	-	Reactive oxygen species
TG	-	Triglycerides
TC	-	Total Cholesterol
T2DM	-	Type-II Diabetes Mellitus
UKPDS	-	United Kingdom Prospective Diabetes Study
VAI	-	Visceral Adiposity Index
VC	-	Vital capacity
VLDL-C	-	Very Low Density Lipoprotein Cholesterol
VAT	-	Visceral Adipose Tissue
W.H.O.	-	World Health Organization
WTHR	-	Waist to Hip Ratio
WC	-	Waist Circumference

ABSTRACT

Background

Iya neerizhivu is one of the types of the Madhumega Noikal. It's maybe correlated with Chronic Obstructive Pulmonary Disease in Diabetes Mellitus. Chronic Obstructive Pulmonary Disease (COPD) is the leading cause of morbidity and mor-tality worldwide. There is evidence to support a connection between COPD and Diabetes mellitus (DM), another common medical disorder. However, additional research is required to improve our knowledge of these relationships and their possible implications. In this study, we investigated the impact of DM on patient outcomes through the clinical course of COPD treated with SEENTHIL Sarkkarai.

Methods

We conducted a prospective open labelled randomized clinical study in patients from the OPD and IPD of Pothu Maruthuvam Department, GSMCH, Palayamkottai Database between April 2016 and June 2018. 40 Patients with Iya neerizhivu were recruited for evaluated the role of Seenthil Sarkkarai in COPD in type II diabetes. The treatments chedule was 30mg/kg body weight for two times per day with ghee for 90 days. Assessed the FBS, PFT changes, MMRC score, and Lipid Profile before and after treatment.

Results

In clinical study 60% of out patients and 55% of In patients showed good improvement 30% of out patients and in 40% of In patients showed Moderate improvement 10% of out patients and 5% of the In patients showed Poor improvement. No adverse reaction was found in this clinical study. The Statistical analysis was done by SPSS statistical package version 20.0. Paired 2 tailed test revealed that the fasting ($P<0.001$) and postprandial blood glucose (<0.001) and HbA1c ($P<0.001$), PFT ($p<0.001$), showed significant reduction after Seenthil Sarkkarai intervention. The trial drug subjected to biochemical and pharmacological studies and gave significant results also. The results suggest Seenthil Sarkkarai to be beneficial for the treatment of Iya neerizhivu (chronic obstructive pulmonary disease in type II diabetes). Further follow-up studies are warranted to confirm the safety aspects of Seenthil Sarkkarai use.

Introduction

CHAPTER-I

INTRODUCTION

1.1 BACKGROUND

Diabetes mellitus is a chronic debilitating and devastating disease. The incidence and prevalence of diabetes mellitus and its complications are increasing day by day. Its complications gives rise to micro and macro vascular diseases which affect eyes, kidneys, heart, blood vessels, nerves and also lungs. Chronic conditions are large in number, the prevalence of each one is high and so does the annual cost of their care. More over, clinicians alert about the impact of one disease on the development and severity of others. Among chronic morbidities the most prevalent are cardiovascular disease (CVD), cancer, diabetes mellitus (DM) and Chronic Obstructive Pulmonary Disease (COPD) (Chillón et al., 2009).

Chronic Obstructive Pulmonary Disease (COPD) and Diabetes Mellitus (DM) are common medical conditions in India. COPD is a progressive, partially reversible airflow obstructive condition and it over burden in developing counties life. In 2020 more predicted that COPD and DM are a third leading cause of death in Asian countries having three times the number of patients than the rest of the world. The mortality and co-morbid conditions like DM associated with COPD is greater impact on health outcomes.

Diabetes mellitus (DM) is Co Morbidity of chronic pulmonary air way disease. A series of studies have shown that DM is associated with impaired lung functions. The chronic complications of Diabetes mellitus includes a number of pathological changes involving different systems and among there, lung represents a target organ for diabetes mellitus micro angioapathy in patients with diabetes mellitus. The Framingham Heart Study is readed that, the association between glycaemic status and reduced lung functions. The diagnosis of DM was associated with lower adjusted mean residual force expiratory volume in one second (FEV1) and forced vital capacity (FVC). The Copengehan Heart Study, a longitudinal analysis, has reveled that an association between a new diagnosis and impaired lung function is more prominent in diabetic subjects treated with insulin compared with subjects treated with oral hypoglycaemic agents.

The association between impaired lung function and diabetes thought to be the result of biochemical changes in the structures of the lung tissue and air ways that

involves various mechanisms like to systemic inflammation, oxidative stress, hypoxemia, or ultimately to the direct damage caused by chronic hyperglycaemia. The lung function decline in patients with diabetic is a consequence itself and diabetic patients seem to have increased risk of several non-neoplastic lung conditions such as asthma and COPD and other airway diseases.

COPD classification by symptoms and spirometry analysis

COPD classification by symptoms/disability		
COPD stage‡	Symptoms	Spirometry
At Risk (not yet COPD)	Asymptomatic smoker or ex-smoker or chronic cough/ sputum	FEV1 ≥ 80% predicted FEV1 / FVC ≥ 0.7
Mild	Shortness of breath from COPD with strenuous exercise or while hurrying on the level or walking up a slight hill	FEV1 60% - 79% predicted FEV1 / FVC < 0.7
Moderate	Shortness of breath from COPD causing the patient to walk slower than most people of the same age on the level or stop after walking about 100 m on the level	FEV1 40% - 59% predicted FEV1 / FVC < 0.7
Severe	Shortness of breath from COPD resulting in the patient too breathless to leave the house, or breathless after dressing or undressing or the presence of chronic respiratory failure or clinical signs of right heart failure	FEV1 30% - 39% predicted FEV1 / FVC < 0.7
Very Severe		FEV1 < 30% predicted FEV1 / FVC < 0.7

Adapted from the Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease - 2007 update.

As per the Siddha perception, according to the classical texts *Noinadal and Noi Mudhal Nadal Part II and Yugi Vaidhaya Chinthamani 800* are clearly illustrated that clinical symptoms of *Iya Neerizhivu.*

Our *Theraiyar* in his "*Theran karisal"* is classified the diseases of the urinary system into two major categories of "*Neerinai Perukkal"* and "*Neerarugal Noigal"*. Any pathology which gives rise to increased urination in quantity or frequency irrespective of the varied causes is included under the heading of *Neerinai Perukkal noigal* or neerizhivu or *mega neer* or madhumegam. Diabetes mellitus is viewed under "*Neerinai Perukkal Noigal*" which produces the symptom of polyuria in the affected individuals. Based on the involvement of the three doshas in the pathogenesis, *Neerizhivu* is categorized as Vali, Azhal and Iyam.

The onset of these general symptoms and signs could be assumed as COPD in patients with Non-Insulin Dependent Diabetes Mellitus. While using the literature to form the hypothesis, my study attempts to quantifu the direct relationship between various levels of insulin resistance and changes in pulmonary function on COPD in a clinical setting.

RATIONALE

Seenthil Sarkkarai is a Siddha herbal formulation taken from the siddha literature. Recently, the plant is of great interest to researchers across the world wide, because the therapeutic and pharmacologically proven that the medicinal properties, like Anti-Diabetic, Bronchodilator, Anti-Periodic, Anti-Spasmodic, Anti-Inflammatory, Anti-Arthritic, Anti-Oxidant, Anti-Allergic, Anti-Stress, Anti-Lipidemic, Anti-Malarial, Hepatoprotective, Immunomodulatory and Anti-Neoplastic activities.

The above mentioned references and the pharmacological research works undergone on the constituents of the trial medicine ***Seenthil Sarkkarai*** is potential effect in the clinical study of the management of DM and COPD. So, the trial medicine is safe for COPD in Type II Diabetes Mellitus Patients.

1.2 AIM AND OBJECTIVE

AIM OF STUDY

To Clinical study about the therapeutic efficacy of Siddha formulation in good glycemic control in COPD in Patients

A. PRIMARY OBJECTIVE

To evaluate the therapeutic efficacy of Seenthil Sarkkarai in Iya Neerizhivu (COPD in Type II Diabetes Mellitus)

B. SECONDARY OBJECTIVES

a. To evaluate the Anti-microbial, Pharmacological activities of Seenthil Sarkkarai
b. To evaluate the changes of siddha parameters in Iya Neerizhlivu.
c. To Study about the prevalence of Iya Neerizhivu in Paruva kaalankal (seasons) and Thinai (Geographical distribution)

1.3 JUSTIFICATION OF RESEARCH

In clinical practice Iya Neerizhivu (COPD in Patients with Type II Diabetes Mellitus) is successfully being treated through the therapeutic application of trial medicine Seenthil Sarkkarai. Therefore it was felt essential to undertake a study to precisely gauge the therapeutic efficiency of **Seenthil Sarkkarai** in clinical management of Iya Neerizhivu.

The clinical study is carried out in Department of Pothu Maruthuvam (PG), GSMC, Palayamkottai. To establish an effective management of Iya Neerizhivu with Seenthil Sarkkarai through an open labelled randomized clinical trial, the following objectives had been drawn.

1. The literatures were collected concerning the aetiology, pathogenesis, clinical features, prognosis and the treatment protocol for Iya Neerizhivu in both Siddha and Modern perspectives.
2. 20 in patients and 20 out patients of either sex with Iya Neerizhivu were screened and selected for the study.
3. The distribution percentage of Iya Neerizhivu under sex, age, occupation, social economical status, personal habits, diet, paruvakaalam and hereditary factors with reference to the clinical study were understood.
4. The therapeutic efficacy of the trial drug on Iya Neerizhivu with the aid of Siddha and modern clinical parameters and the prognosis of the disease were assessed.
5. The potency of the trial drug through evaluation of Biochemical, Microbiological and Pharmacological analysis was carried out.

Review of Literature

CHAPTER-II

REVIEW OF LITERATURE

2.1 SIDDHA ASPECT – NEERIZHIVU

In the Siddha system of medicine all creation and genesis of matter on earth are controlled and regulated by the Pancha Bhootas, and it based on Tridoshas and Dasa naadigal at Microcosm and Macrocosm plane, an imbalance in the creative forces subsequently causes defective function, affecting the existence, qualitatively and quantitatively. Our ancestors elaborated the knowledge of the disease Neerizhivu in many school of thoughts. Saint Theraiyar in his *"Theran Karisal"* has classified the diseases of the urinary system into two major categories of "Neerinai Perukkal" and "Neerarukal Noigal". Any pathology which gives rise to increased urination in quantity or frequency irrespective of the varied causes is included under Neerinai Perukkal Noigal. Diabetes mellitus has also been viewed under "Neerinai Perukkal Noigal" which produces the symptoms of polyuria.

The different classifications of Neerizhivu which have been documented based on the observations of the complaints of the patients. The classification of Neerizhivu has been disclosed by Yugi muni in *Yugi Vaithiya Cinthamani 800*, Agathiyar in the text book of *Agathiyar Kanma Kandam*, Theraiyar in *Theraiyar Vaagadam* and Thirumoolar in *Thirumoolar Vaithiyam 600*.

2.1.1 ,ay (DEFINITION OF NEERIZHIVU)

Neerizhivu is a disease characterized by frequency of passing urine (polyuria), presence of honey odour in urine on heating. It ultimately deteriorates all the seven Udal thathus (seven fundamental tissues of the body)

', dpggh d ,dpggyy < tejhLk
xU Jsptha tpllhhi fg gpzpaha Njhd Wk"

- FUehb

'm z ikahabf fbfF ehpwqF

kbffbfF miuehoÍ jdÍNy fhZk
ntz ikahd jbajdÍwwhd gÍbfFk
kÍffhd rlk ntS jJ NkdÍ fdWk"

-AÍfÍ itjjÍa rÍejhkzÍ-800

2.1.2 Nehatuk toÍ (ETIOLOGY)

The etiological factors described by various siddhars are,

i. Excessive sexual activity.
ii. High fat food.
iii. Chronic alcoholism.
iv. Obesity
v. Physical inactivity
vi. Psychosomatic stress
vii. Genetic factors are lead to neerizhivu.

'Nfhijah fytÍNghij
nfhOjjkd ,iwrrÍNghij
ghJtha neaAk ghYk
ghÍTld czguhfÍy
Nrhj ghzLUt kÍff
RffÍy gÍuNkfejhd
xJ ehÍoÍT Nru
Tznld mwÍeJ nfhsNs"

-mfjjÍah-1200

The same also discussed in "*Yugi Vaidhya Cinthamani*", Yugimuni in his text attributes this disease due to injudicious diet containing high fat, sweet. Too much of sedentary habits without exercise also leads to neerizhivu, undue fear, severe depression has also emphasized for the development of Neerizhivu noi.

"cwgtÍfFk ghy neaahy ,iwrrÍ fsshy
ThÍiraha kdjddha mUtÍUej
kwgtÍfFk gjhhjjjjhy kJut]jhy
kejqfs jidGrÍjjy Ntfhggzlq
Fwgtfk FSjj tddkqif Nfh\b
FwÍjj eÍjjÍiu jtÍhjy mffÍdÍkejk
jwgtÍfFe rhuejhd kÍfggUjjw

rQryejhd kpfggajjhy jhpfFk NehNa”

- A+f p i t j j pa r pejhk z p-800

2.1.3 Neha v z (CLASSIFICATION)

Basically, Neerizhivu is the disease associated with and increased frequency and quantity of urine. The below twenty varieties are described in the works of almost all the Siddhars. Out of these twenty different kinds of Neerizhivu, four are caused by Vatham, six are caused by Pitham and the remaining ten are due to Kapham.

The following quotations describe, twenty different kinds of urinary disorders on the basis of colour, consistency, taste, smell, weight etc.,

‘c l b z Nuhf j jhYk KWkngUk gr pa pdhYq
f l l t po Nfhi jkhjh fy t pk lbyh i kayhY
K l lwh ehYkhW K d%dW nkhdW nkdW
j pl lkha tUtnjdW j pUkK d paUs pr nrajhh”

- mf j j pah-1200

‘myY nkdNw NkfkJ ,uz Lgj J
kf poeJ eNf S nkdW t rd pjjhNu”

- a+f p i t j j pa r pejhk z p-800

‘t rd pjj NkfkJ ,uz L gj J
thj j pw g pwejryk ehNyahFk
g pr d pj j g pj j j p Ywg t pj j
Nguhd ryejhD khW khFk
Njrd pj j NrlLkj j py cwg t pj j
ruhd ryejhD gjNj ahFk
,rd pjj ,jDila F zh F z qfs
vo pyhd cwgj j pa pakgf NfNs”

- a+f p i t j j pa r pejhk z p-800

Neerizhivu caused due to deranged vatha dosham (t s pf Fwwj jhy tUk Nkfeh Neha) are 4 types. Namely with synonyms,

i. Achiya megam (nei mana neer)
ii. Suththa megam (pasu mana neer)
iii. Pramiya megam (oon mana neer)
iv. Mangisaravi megam (Elamarik kozhuppu mana neer)

‘jhpjjplll thjjjpd ryejh dhY
jdpahd ehY fFk NgNu njd dpy
mhpjjplll Mrrpanfejp Nkfj NjhL
mjdgpwF Rwwkh Nkf nkhdW
Nguhd khqfprutp Nkfnkhd W
Fwpjjplll ,J thj ryejhdhY
F zhF z jjpDlgnkyyhk Fwpggha NfNs”

- a+fp itjjpa rpejhk zp-800

Neerizhivu caused due to deranged pitha dosham (gpjjf Fwwjjhy tUk Nkfeh Neha) totally six in numbers. They are,

i. Appiya megam (yanai matha neer)
ii. Apiramiya megam (kattralai mana neer)
iii. Sampirna megam (chunna mana neer)
iv. Mathumiya megam (thithippu neer)
v. Asaththiya (palingu mananeer)
vi. Arkka megam (muyatkuruthi neer)

‘Kiwahd gpjjry khW khFk
Kjpuej mggpankdWk gpukpa nkdWk
Jiwahd rhkguzk Jkg nkdWk
rhjjpfNt ahtpUjj jdNdh lhW
kiwahd tpejhW Nkfe jd id
kfhNjtH nrhyyplNt Njtp Nflfj
Jiwahd F zhF z jij tpujJr nrhyy
Rwwkh aggpajjpd R&gq NfNs”

- a+fp itjjpa rpejhk zp-800

Neerizhivu caused due to deranged kapha dosham (fgf Fwwjjhy tUk Nkfeh Neha) totally ten in numbers. They are,

i. Vasa megam (vasa neer)
ii. Uththama megam (theli neer)
iii. Machcha megam(moolai neer)
iv. Akiha megam (ela neer)
v. Surari megam (kal neer)
vi. Sikkila megam (thavala neer)
vii. Udhaha megam (kalu neer)
viii. Pinani megam (then neer)
ix. Lavana megam (uppu neer)
x. Thayiththiya megam (eraichchi neer)

‘Mwhd r‰Nylgrykgj J jdid
Muz nrhy ythjjhs jhd NflFk NghJ
thwhd trhNkfk cjjk Nkfk
krr‰ah Nkfj Njhlh ff Nkfk
J}whd Ruhu‰Rfy Kjj Nkfk
Rwwkhk g‰dhd‰NahL ytz Nkfk
Njwhd nja‰jj‰akh Nkf nkdW
nrgg‰dhh r‰Nylgjj‰d nryjJj jhNd”

- a‹f‰ itjj‰a r‰ejhkz‰-800

2.1.4 Kw Fw‰F z qfs (PREMONITORY SYMPTOMS OF NEERIZHIVU)

In Siddha we can find the description of early symptoms of the disease. They are voracious appetite, excessive thirst, weight loss, polyuria, insomnia, anxiety, and striae of the skin all over the body due to sweating, exertion and fatigue.

‘rh‰ahf Nkfjjhy mghd thA

jhd GiffF NkNywpf fghyr#lhk
nghpjhd Nkfjjhy mjjpnteJ
Nghkggh jirnteJ ujjk twwpg
ghpthfpj jrthAthy kejqnfhzL
ngUejdp kygejk cjhd thA
thpthfpj Njfnkyyhk tpleuhNy
nkaaopej Nkfnkdw jpUgjhrNr"

- rpjj kUjJtk

According to Dhanvanthiri Vaithyam Part-II, which is given some other premonitory symptoms like burning sensation in hands and feet, itching, frequency of thirst, polyuria etc.

'kzlye jddpYss khjhfFkGUlhfFq
nfhzlNjhh ryffoprry nfhsSKd fhZNehafs
fzbL Kly fhy iffs fhdwoe njhpeJ fhejp
Azleh Rtwpf fhlbAileJeh fopAnkdNw"

- jdtejph itjjpak

2.1.5 FwpFzqfs (SIGNS AND SYMPTOMS OF NEERIZHIVU)

Yugimuni has described the common symptoms and signs of 20 types of Neerizhivu as followed,

- Excessive Urination
- Excessive Thirst
- Excessive Appetite
- Cough
- Dry mouth
- Tiredness
- Fatigue
- Irritability
- Fluctuation of weight
- Blurring of vision, nausea, headache
- Burning and spasmodic pain in urethra and dull ache in testis.

- urine may be cold, slimy to touch, brownish yellow in colour and produces white sediments
- Ants and flies are attracted to the site of voided urine
- When the urine is heated it gives honey odour

‘$whd NkfkJ ,UgJfFk
Fzejid rptdnrhyy Njtpnflf
jhwhd jhfnkhL Nrhf Nkfe
jhpahky ehpopjy ,Uky %rR
Mwhdmurp rjjp rpjj gpuik
mbffbfFj jz zh jhddq Nflly
<whd ,LgGfs fLgG fhzy
vYkG owwyowwNyh nlhpTzlhFk”

‘vhpNthL rhunkyyh kiwgllhw Nghy
vopOlkG Nehjy epjjpiuapyyhik
kdJ rQryggLjy fhwWNtzly
nkhpNthL Nky%rR kpfTzlhjy
tpffnyhL kaffejhd nkjjf fhzy
njhpNthL Njfnkq Fk ntSUzljhy
Njfnkjj thNyhgggLjy fhNz”

‘jz ikaha ryejhDk gRgG kQrs
jhdpwqFk grKk NfhrKq fLfFk
mzikahabf fbfF ehpwqFk
mbffbfF miuehop jdpNy jhZk

‘ntz ikaha abajdpwwhd gpbfFk
kpffhd rlkntSjJ Nkdpfdwk
gzikahag gQthzljdpw nfhyYk
gfphfpdw kJNkfjjpd ghqF jhNd”

- afp itjjpa rpejhkzp-800

In *Agasthiyar Aayulvagadam* signs and symptoms of neerizhivu little vary with above and are mentioned like,

- Burning sensation on hands, legs
- Dryness of mouth
- Giddiness
- General weakness
- Tiredness
- Tremors
- Loss of appetite
- Sweating
- Pallor of skin

‘K fNk fhej neQRyheJ KWj J
K l Y eL q f efNk gu eJ rh ne f oeJ
eQR z l th Nghy Nj fk NrhheJ g f Yk uT KU f fAl y
g f WNk d Ak j sheJ k fNt j ht z K z lhFk”

- m f] j aH MAs th f l k

2.1.6 Common Sign and Symptoms of Vali, Azhal and Iya neerizhivu

Saint Yugi clearly described the 20 subtypes of Neerizhivu the different clinico-pathological conditions produced out of specific doshas and saptha dhathus showing gross urinary characteristics and clinical manifestations, and also prognosis of the disease if left untreated.

Table shows clinical features of different subtypes of Neerizhivu

Doshas	Types	Specific Signs	Common Symptoms of Doshas
Vali Neerizhivu			
1.	Nei Mana Neer	• Urine contains colour of ghee, stickiness and ghee smell. • Polyuria • Weight loss • Death occurs 7 days after disease appeared.	• Burning sensation of hands, feet and face. • Dryness of mouth • Black discolouration of teeth, tongue and throat. • Difficulty in speech • Giddiness
2.	Pasu Mana	• Urine likes cow’s urine and	

	Neer	smell • Polyuria • Weight loss and fatigue • Death occurs 15th day after disease appeared.	• Excessive Thirst • Excessive Appetite • Ache and pain all over the body
3.	Oon Mana Neer	• Polyuria • Smell like blood • Gives honey odour when burned • Killed in 6 months	
4.	Elamarik Kozhuppu Mana Neer	• Urine contains particles of flesh and membrane • Give smell of Billy meat washed water (pink). • Polyuria • Death occurs 3-8 days or 5th month	

Azhal Neerizhivu			
1.	Yanai Matha Neer	• Simile of such patients is given with adult elephant as regards passes of urine. • Sediment like sea sand if boiled • Killed in 6 months	• Burning sensation in all over the body • Emaciation • Excessive perspiration and bad odour • Urine passes like pus, honey, aloe juice • Burning in urethra, scrotum, liver and stomach
2.	Kattralai Mana Neer	• Polyuria • Aloe smell • Gives putrid odour when boiled • Killed in 3 years	
3.	Chunna Mana Neer	• Urine is like an alkali (ash) solution, in smell, colour and touch. • Killed in 2 years	
4.	Thithippu	• Frequency of micturition	

	Neer	• Pain in urethra • Honey smell when boiled • White colour sticky precipitation in bottom • Pallor of the body • Killed in 5 years	
5.	Palingu Mananeer	• Dysuria • Quality of urine is turbid & slimy. It is sticky & threads may be demonstrated like gum. • Killed in 5 years	
6.	Muyatkuruthi Neer	• Frequent and excessive micturition • Urine red in colour like hare's blood and meat smell. • Dysuria • Killed in 9^{th} month	
Iya neerizhivu			
1.	Vasa Neer	• Urine contains fat (vasa) and smell • Pain in penis and scrotum • Death occurs within 7 years	• Obesity • Pallor of body • Skin rashes like itching, ulcers and allergic rashes • Excessive Thirst • Excessive Appetite • Cough • Sputum collection in throat
2.	Theli Neer	• Clear urine in larger quantity without odour, feels cold sensation while passing urine. • Killed in 10 years	
3.	Moolai Neer	• Urine seems to like contains bone marrow (majjai). • Polyuria • Putrid smell • Life span-5 years	
4.	Ela Neer	• Urine like tender coconut water	

		and smell. • Gives coconut oil smell when boiled • Polyuria • Weight loss • Thirst • Anxiety • Killed in 7 years	
5.	Kal Neer	• Urine-white in colour and frothy like toddy and smell. • Fatigue • Killed in 7^{th} year	
6.	Thavala Neer	• Patient passes urine similar to quality of semen or semen itself may be mixed with urine. • Black colour sediment like liver after boiled • Killed in 3 years	
7.	Kalu Neer	• Urine incontinence present • Precipitation like lime of conch • Body odour present • Killed in a year	
8.	Then Neer	• Enormous urine output like honey and smell • Sediment like wax • Ants and flies are attracted to the site of voided urine • Honey odour present in body • Killed in 5 months	
9.	Uppu Neer	• Urine seems to be salty and white and it's odour. • Polyuria • Alkali ash precipitation • Sediment salt when boiled • Weight loss, worries, loss of appetite, and indigestion • Killed in 15 years	
10.	Eraichchi Neer	• Urine red in colour and smell like meat washed water. • Dysuria • Polyuria • Killed in 3^{rd} year	

ts;fFwwjjhy tUk Nkfeh Neha:

‘Mrnrdwehykkq Fzjijf Nfsh
aofhd iffhyfz Zlyowwk
ehrnrdwehtwSkgyY ehfF
eLjnjhzil fWgNgW Kjnyl lhejhd
NgrnrdwehtwSkgyY ehfF
eLjnjhzil fWgNgW Kjnyl lhejhd
Ngrnrdwg;yr\akhq fzNky NehfFk
ngUftddejz zUk;fNt thqFe
jhrnrdwrhuejhd fjj;ntlLj
jhdNghyf fLjJNk joY zlhNk”

- a+f; itjj;a r;ejhkz;-800

moy Fwwjjhy g;wfFk Nkfeh Nehafs:

‘mw;aNt g;jjrykhWNk jhd
mqfkj;wnraf;dwFzjijf Nfsha
jw;aNt clytww;vh;Tzlhfk
rljj;Yejhd eh;Yejhd ft;rRzlhFk
njw;aNt rgNghYq fwwhio NghYe
NryNghYe NjdNghY ehwwKzlhk
ntw;aNt grjj;wNfhrjj;y Fjjy
k;Fkuy ehg;a;Yk Ntffhlhnk”
‘Ntffha t;uzKzlha thajhdhYk
t;ffNyhL mUj;ahar RuKzlhFk
jffhlha Njfejhd f;lfnfhllhJ
j;affnkhL %hrirAzlhkaffkhrNr
rhffhlha ehtwSqfz zhjhfQ
rhj;nahU rhunkyhe jshrr;ahFe
jhffhlha kyryejhd k;fTzlhFe
jhffhlha kyryejhd k;fTzlhFQ
rkFzejhd g;jjry khWkhrNr”

- a+f; itjj;a r;ejhkz;-800

lafFwwjjhy gpwfFk NkfehNehafs:

‘jrkhd gjJfFq F z j i j Nfsha
rhuejhd gUjJNk nt SgG z lhFk
mrkhd jpdT z lh kbffbfF
frkhd tpUkYld Nfhio Az lhq
fd thpth ahahr Koiyah Fq
Frkhd F z qfisnayyhk rpNylLke jddpy
nfhba ryfF z nkdW $wpdhNu”

- a+fp itjjpa rpejhk z p-800

2.1.7 KfFww Kjypa NtWghLfs (PATHOGENESIS)

The direct inference from these poems is that all Siddhars attribute diabetes mellitus mainly due to excessive indulgence in sex which results in total loss of body strength as a whole including the nervous system. Due to the intrinsic, extrinsic and other causes tridoshas are affected. Initially the pitha dosham has vitiated and causes burning sensation of the body and altered vayus also. According to this Kapham and Vatham are deranged and udal kattugal get disturbed to do their normal functions. Gradually body become emaciated and essense are excreted through urine. The severity of the disease is measured by the functions of three doshas and seven thathus. Debilitation and other sequence of disease will be occurring due to loss of appetite and loss of body strength. This as follow,

According to the below references , the nourishment of Saptha Dhathus loosen and excessive discharge of the urine containing sweetness accompanied by thirst together with loss of strength is an important characteristic feature of the Mega neer.

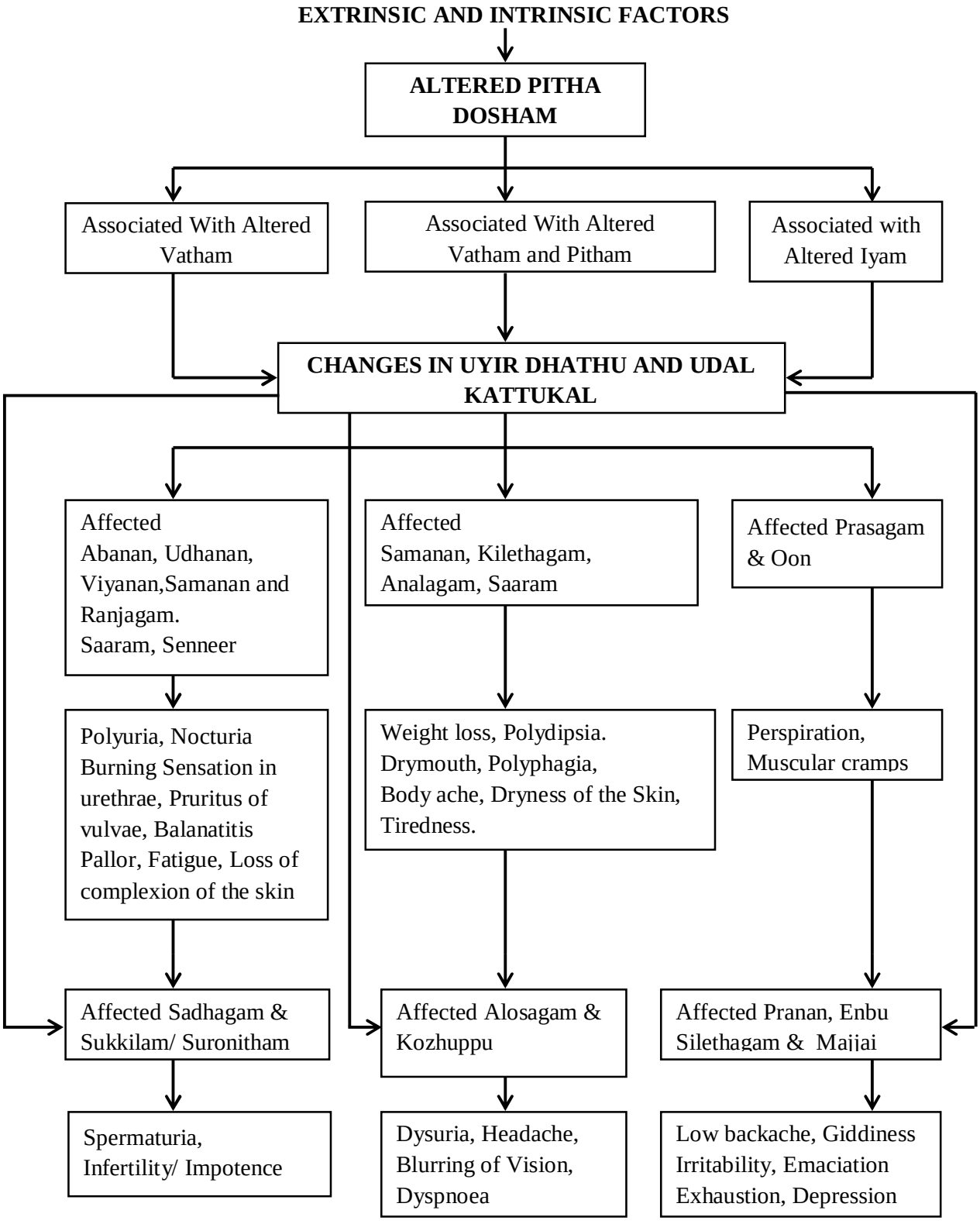
‘gfhgpjj tpeijayhJ Nkfk tuhJ”

- Njiuau

‘FwpAlNd Nkfejhd
nfhLiknraJ
FiweJtUe jhJntyyhq
Fdwpgnghfk”

- gjpnzd rpjjh ehb E}y

PATHOGENESIS OF NEERIZHIVU



2.1.8 kJNkf Nehaµy fhZ kgjJ t if mtjijfs
(COMPLICATIONS OF THE DISEASE)

Saint Yugi well elaborated in the text book of *yugi vaidhya chinthamani*, the onset of the following sufferings as avathaigal will be followed gradually if the disease is not controlled or left untreated.

Avathai-1: Progressive weight gain and dilatation of urinary meatus

Avathai-2: Excessive urination, disorder of semen (polyuria, Asthenospermia)

Avathai-3: Dryness of the tongue and gaseous abdominal distension (polydipsia, and diabetic gastro enteropathy)

Avathai-4: Excessive thirst may leads to excessive fluid loss (Encephalopathy, polyphagia, Diabetic metabolic encephalopathy)

Avathai-5: Frequency of urination, spermatorrhoea (chronic renal failure)

Avathai-6: Patient awakening in bed, breathlessness (metabolic syndrome)

Avathai-7: Recurrent nausea with vomiting, breathlessness (metabolic Syndrome)

Avathai-8: Chronic ulcer, abscess or carbuncles are present in body (Diabetic Ulcer)

Avathai-9: Immoral behaviours, watery diarrhoea (Superadded opportunistic infections)

Avathai-10: Pulmonary and extra pulmonary tuberculosis

‘fhz Nt Kjytjijr rhue jhDq
fdkhfg gUjjµWfµ ehjJ thuk
Ntz Nt Ntz lhffµafykgz Z
kµfftuz lhktjij tµskgf Nfsha
%z Nt %jjµugg ilAkhr Rfy
KfKOfµj Njr[Rjhd kµfNt FdWk
ehz Nt %dwhF ktjijf Fjjhd
ehtwSk thAtJ kWe jhNd”
‘jhdhd ehytjij aqf jhfQ
rddµaJ ghjKz lh ike tjijj
Njdhd eh ngUFe jhJe\lk
eµiyahw ktjijAlw fµilnfhsshJ

%dhd %hr i r tU Nko t j i j
k‰f f tNuh f rQR thre Njf rhlbak
Vdhd v l lht j t j i j jhNd
vOf‰uej‰ g‰s i t Aejhd k‰fT z lhNk
c z lhF nkhdgjh k t j i j f Nfsha
coffhd tj‰rhuq f‰Uk‰ A z lhk
g z lhd gj jhejh i t j i j Nfsha
ghukhk raqf z L gujJf NfFk"

- a+f‰ i t j j‰a r‰ejhk z ‰-800

According to the different school of thoughts, the above 3 avathaigal will be cured with medicines and up to nine avathaigal can treat.

2.1.9 jUk juhj i t (PROGNOSIS OF THE DISEASE)

Disease is always producing the imbalance between the ratio of Vatham, Pitham and Kapham. This imbalance affects the five vayus (abanan, udhanan, viyanan, samanan, pranan), seven udalkattukal and slowly affects the appetite. An imbalance in Kapham does imply an imbalance in the other two doshas too, and contribute in further destruction of the system.

According to Yugi, the 20 types of megam also could be further divided in three categories as prognostic classification as below,

1. **Sadhyam (Manageable) -** Kapha megam (10)
2. **Yapyam (Palliative) -** Pitha megam (6)
3. **Asadhyam (Unmanageable) -** Vatha megam (4)

'nraaNt trr‰ukhe j z l khd
nrakhd KJFjj z i lg gww‰ e‰wFk
ngaaNt ngUeukg‰y Nkfe jhDk
g‰wfFnkdNw jhdw‰eJ thje j d dhy
g‰aaNt g‰wdejryk ehy rhj j‰ak
g‰j j j j‰w g‰wejrykhWk ahgak
i faNt NrlLkj j‰w g‰wej gjJk
gukD iuj jhhrhj j‰ak guhg h‰fNf"

- a+f‰ i t j j‰a r‰ejhk z ‰-800

Even though some sequence of disease will be occur in madhumega disease, it also incurable, if associated with Diarrhoea, Excessive swelling in the Body, Tuberculosis, Excess Breathing, Hiccough, Abdominal Pain, Abscess etc.

‘ehNehapd; yj;rhuK
d;kht ff k;isgG
khh%rRwy t;ffybf
fbNatuy ta;ww;y
NrhNehNahL g;sitt uy
juhfFw; nadNw
ehhnfhz Liwnrajhh;ij
edwhaw; thNa”

- fz Zrhk;ak

The patient is sure to die if Neerizhivu associated with Vatha diseases, griping of the Stomach, Excessive Accumulation of Gas, Hiccough, Dyspnoea, and Asthma stated in the Sathaga Nadi,

‘Jj;gghd Nkfjj;y eu;o;T khfh
Njhdw;ae h;o;Tjd d;y thjK khfh
kj;gghd thjjj;y ta;wWisrr yhfh
tUKisrry jd d;ythA nfhOjJ khfh
nfj;gghd thatj;Ny t;ff yhfh
$zlt;ffy jd;y;isgG nfhOjj yhfh
Fj;gghd ,isggj;Ny Rthrk teJ
fyejhYk kuzk vdW fUjyhNk”

- rjf ehb

2.1.10 Neha fz;gG (DIAGNOSIS OF THE DISEASE)

In Siddha System of Medicine Eight different parameters of diagnosis have been devised to establish the exact underlying pathology known as envagai thervu (Nadi, Sparisam, Na, Niram, Mozhi, Vizhi, Malam and Moothiram) and confirmation through interrogation.

‘ehbggh;rk ehe;wk nkho;t;o;
kyk %jj;uk;it kUjJ tuhAjk”

- Njiuah

- **Nadi Nadai (Reading of Pulse)**
  - ❖ The most important parameter of diagnosis is Nadi.
  - ❖ In Thirumoolar Naadi, it is quoted that when the three Vatha, Pitha and Kapha naadi are feeble, the corresponding derangement in the doshas leads to Neerizhivu.

‘ghhj j‰L %dWk gj‰eJ nky‰eJ e‰wf‰y
Njhej‰L Nkfk teNjhdw‰Na nghUej‰ nkaa‰y”
- j‰U%yh ehb

In other way Thirumoolar said, the Pitha and vatha variation is indicated clinically by excessive hunger, thirst, emaciation and passing of large quantities of urine with sweet taste.

“,Uk‰a g‰j jKk thjKk $by
kUTy Nkfk thUj‰ NghyhLk
cUtk Ntnwh U Kz lTlw fhaej‰Lk
cUfNt t+NdhL cw‰Qr‰ ,d‰fFNk’
- j‰U%yhehb

Thirumoolar also states that when Vatham combines with Kapham, the consistency of the urine becomes like toddy with emaciation of the body and pallor as seen in chronic cases. It is also known as “Kudila Nadi” (Like movement of worm).

‘,d‰ff‰dw thjj j‰il Nrh‰y laejhd
gd‰ff‰dw fs Sggj d‰Nghy eNuhLk
fd‰ff‰dW Nkd‰ fiueJ nt SgNgWk
fd‰fFkJ Nkfe jgNghi jaNk”
- j‰U%yhehb

In Thirumoolar nadi and Parioorana nadi are quoted that, in the developed stage of the disease the vatha, pitha and kapha nadi will be feeble.

‘ghhj j‰L %dWk gj‰eJ nky‰eJ e‰wf‰y
Njhej‰L Nkfk teNjhdw‰Na nghUej‰ nkaa‰y”
- j‰U%yh ehb

‘Ju z K l d ehgghL n f hggg ghl h z hw
n rhy Y f⇩Nw d ehbnayyhe f o dW f h Z k”
- gh⇩g+u z ehb

‘ehNk f kh d th f F ehb jhD k
ehkakha ehbnay yhk gyNk n f l L f
f hhNk f k NghNy t e n jh⇩Nky Gu z L
t⇩OkGOg NghyN t Gu z L f hl L k”
- gh⇩g+u z ehb

The aggravation of Pitha naadi is seen, it leads to excessive burning sensation and indicate mega neer.

‘gwg⇩b f f Nk f k v d why g⇩j j kWk
ghy f Nd f hq i f n f h z L euhk ghNu”
- gh⇩g+u z ehb

- **SPARISAM (SENSATION OF PATIENT DURING TOUCH)**

Warm, dry, pricking pain all over the body especially palms and sole are the features can be found on madhumega disease.

In mega neer due to Vatha, Pitha and Kapha dosham, have burning sensation in hands, feet, eyes and face and also fever.

- **NA (EXAMINATION OF TONGUE)**

In tongue examination following things are should be consider as follows,

❖ Niram (colour)	-	Pale in kapha neer
		Black in vathaneer
		Yellow pitha neer
❖ Thanmai (character)	-	Dry and fissured
❖ Pulan (sense)	-	Saliva tend to taste sweet
❖ Umizh neer (salivary secretion)	-	Reduced

- **NIRAM (EXAMINATION OF COLOUR AND COMPLEXION)**

It is different from their original complexion on the skin. In madhumega disease pale or dark complexion is common.

- **MOZHI (EXAMINATION OF SPEECH)**

Speech due to increase of pitham, the patient is likely to suffer from tiredness and giddinees, therefore the bound of speech become low pitched.

- **VIZHI (EXAMINATION OF EYE)**

In neerizhivu visual disturbances (blurring of vision, glaucoma and cataract) may be present and following things also should consider,

- ❖ Niram (colour) - red/pale
- ❖ Thanmai (character) - dry
- ❖ Pulan (sense) - reduced touch sensation impairment in vision

- **MALAM (EXAMINATION OF STOOL)**
  - ❖ Niram (colour)
  - ❖ Nurai (froth)
  - ❖ Elagal / Erugal (consistency) are should be consider in examination of stools. When Vatham is in high proportion there is constipation, with increase of Pitham there exists diarrhoea and increase in Kapham results in white, milky motion.

- **MOOTHIRAM (EXAMINATION OF URINE)**

Urine examination is done under two categories,

a) Neerkuri (The common nature of urine)
b) Neikuri (oil drop method)

a) Neerkuri (The Common Nature of Urine):

The following points have to be taken into account in the urine examination:

- ❖ Colour
- ❖ Weight and density

- Odour
- Froth
- Quantity

‘tej ehffhp vil kzk Eiu vQrnyd
iwejpaYs tit aiwFJ Kiwna”

According to many schools of thought well described the nature of urine in 20 types of madhumega disease. The common features of neerkuri are following,

- Niram (colour) - crystal clear urine
- Weight and density - thickening of the urine
- Manam (odour) - honey smell
- Nurai (froth) - increased
- Enjal (deposits) - small deposits in urine

If the urine is crystal clear, it indicates the vitiation of kapha in which the prognosis is said to be very bad.

‘nt z ikAwW kpfj njspTiljNjy
cz ikahe Rjj rjsj Jjfkhh
,eehg grgglhjpjt Dila aejuk
Keeh ngUffkopthd cajnthfFNk”

-NjiuaH eHfFwp neafFwp

b) Neikuri (Oil Drop Method):

A drop of gingely oil is dropped in to a wide vessel containing the urine to be tested and kept it under the sunlight. The variations of three doshas in disease can be diagnosed by the shape of gingely oil on the surface of urine. It gives the details of prognosis of the disease.

If the observed pattern like as head structure or human or body and of kamandalam, then the patient has the ability to get cure of diabetes.

‘FwpaJNf Sk eupy Fiwjjiy NghYe Njhdwpy
gpwpejpLKliyNghYk ngUq fkz lykNghyjhDk
twpejplrrhjpakkjhk typgpy kDNthHfnfdW
nrwpejpLKdpthjhKQ nrggpaFwpggjhNk.”

-afpKdp itjjpa fhtpak

If the observed pattern like as circle or thoranam i.e hanging decorations shape, then it cannot be treated and classified as incurable (mrhj jpak).

‘ifapdpnyz iz thqfp fopej eujd dpwF jj
nrajJtllkhFQ NrUeNjhuz kNghyjhDk
IaKkpyiyfz lha rhjjpakyyntdW
JaaedKdpthjhDQ nrhyypaFwpggjhNk”

-afpKdp itjjpa fhtpak

According to *Thanvanthiri Vaithiyam*, which is given elaborately about the shapes and their prognosis of the main three types of madhumega disease are follows,

Vatha Neer:

‘%isAkepz KkNghy Kwpej Rffpyk Nghy
Mshp NtYqNfhY kz qfDk mkGNghy
espa eukGNghy ehjdpnyz nza fhzpy
thspid ntdw fz zhathjjjpd $WjhNd”

-jdtejph itjjpak

The above stanza says that if the oil drop is like the brain or lymph or fractured sperm or sword or Cupid’s bow or long nerve is indicated features of vatha type of neerizhivu.

Pitha Neer:

‘igautyFy khNj ghUs NshHfpopej ehpw
ifapNynaznz thqfpf fopejNjhh JUkghwFjj
ikaWNkdpnahjj tllQ nrajpUfFkhfpy
maAW eujhF kyyjhwgpjjkhNk”

-jdtejph itjjpak

When the oil drop is made dark colour circle it is a symptom of pitha type of neerizhivu.

In the text book of Siddha Maruthuva Noi Thoguthi-I, Megaroga Nithanam well defined the prognosis of the types of madhumega disease,

- ❖ The oil drop doesn't spread and placed like circle of eye and then adhere to the mouth of the dish is indicate the disease curable.
- ❖ When the oil drop sinks into the bottom and given sudden spread then oil and urine mixed is known as incurable.
- ❖ If the oil drop has appeared in the surface of the urine it indicates Kapham, if it is hide its Pitham and it is going to sink known as Vatham.

'ghuha eh gh z l j j ɒy ghq fha j ɒd Nky eyny z n z a
ruha xU Js ɒ t ɒl lhf fhy r ɒjw ɒ Xb Nghfhky
Neuha e ɒdW f z t l lk Nghy neUq f ɒ r lb tha vq Fk
Nru neUq f ɒ e ɒHf f ɒYNk jUk , jwF kUeJ nraNa

nraAk t i faJ Nf sha r ɒwej euj ɒNy v z n z a ɒl lhy
igaa fNo jhoej ɒbDk gjw ɒ Xb r ɒjw ɒbYk
neaAk eUk x dwhf k ɒfNt $b f yej ɒbDk
caAk t i faJ juhJ c j j kk vyyhk k j j ɒgNk

i fa ɒdhy v z n z a thq f ɒ fo ɒej eh j d d ɒy Cww ɒ
xaAw ɒy lakhFk xo ɒej ɒby g ɒj j khFk
nkaAWk v z n z a jhs ɒy k ɒFej NjhH thj khFk
nghaayy , k %dWf Fk Gj j ɒaha mw ɒeJ ghNu"

- NkfNuhf e ɒjhdk-r ɒj j kUj J t njhF j ɒ-I

2.1.11 Nehaff z ɒgG t ɒthjk (DIFFERENTIAL DIAGNOSIS)

- Theli Neer (Diabetes insipidus)
- Neer Kiricharam (Urinary Tract Infection)

2.1.12 kUj J tk

In siddha the management of a disease not only depends on the medicine but the modification of food, habits, and lifestyle also. There are several medicines said in the literatures and practiced successfully by Siddha practitioners. The regulations in food, daily habits etc. are the specialty of most of these medicines.

2.2 MODERN ASPECT - DIABETES MILLUTUS

2.2.1 Definition and description of diabetes mellitus

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Several pathogenic processes are involved in the development of diabetes.

These range from autoimmune destruction of the pancreatic b-cells with consequent insulin deficiency to abnormalities that result in resistance to insulin action. The basis of the abnormalities in carbohydrate, fat, and protein metabolism in diabetes is deficient action of insulin on target tissues. Deficient insulin action results from inadequate insulin secretion and / or diminished tissue responses to insulinatone or more points in the complex pathways of hormone action. Impairment of insulin secretion and defects ininsulin action frequently coexist in the same patient, and it is often unclear which abnormality, if either alone, is the primary cause of the hyperglycemia.

Symptoms of marked hyperglycemia include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision. Impairment of growth and susceptibility to certain infections may also accompany chronic hyperglycemia. Acute, life-threatening consequences of uncontrolled diabetes are hyperglycemia with ketoacidosis or the nonketotic hyperosmolar syndrome.

Long-term complications of diabetes include retinopathy with potential loss of vision; nephropathy leading to renal failure; peripheral neuropathy with risk of foot ulcers, amputations, and Charcot joints; and autonomic neuropathy causing gastrointestinal, genitourinary, and cardiovascular symptoms and sexual dysfunction. Patients with diabetes have an increased incidence of atherosclerotic cardiovascular, peripheral arterial and cerebrovascular disease. Hypertension and abnormalities of lipoprotein metabolism are often found in people with diabetes.

2.2.2 Epidemiology

The mortality rate of diabetes mellitus is high and is ranked in 5th amongst the ten major causes of death in southern part of India. The rising prevelance of diabetes is associated with industrialization and socioeconomic development. The prevelance of diabetes in adults globally is estimated to be 150 million and this figure is expected to double by 2025. Although the prevelance of type-I and II diabetes mellitus is increasing worldwide. The prevelance of type-II diabetes mellitus is expected increase more rapidly in future because of increasing obesity and reduced physical activity. The WHO estimates that 75 per cent of the 300 million adults with diabetes in 2025 will live in devolopig countries.

2.2.3 Classification of diabetes mellitus

Etiologic classification of diabetes mellitus:

I. Type-1 diabetes (β-cell destruction, usually leading to absolute insulin deficiency)
   A. Immune mediated
   B. Idiopathic

II. Type-2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)

III. Other specific types
   A. Genetic defects of β-cell function
      1. Chromosome 12, HNF-1α (MODY3)
      2. Chromosome 7, glucokinase (MODY2)
      3. Chromosome 20, HNF-4α (MODY1)
      4. Chromosome 13, insulin promoter factor-1 (IPF-1; MODY4)
      5. Chromosome 17, HNF-1β (MODY5)
      6. Chromosome 2, *NeuroD1* (MODY6)
      7. Mitochondrial DNA
      8. Others
   B. Genetic defects in insulin action
      1. Type A insulin resistance
      2. Leprechaunism

3. Rabson-Mendenhall syndrome
4. Lipoatrophic diabetes
5. Others

C. Diseases of the exocrine pancreas
1. Pancreatitis
2. Trauma/pancreatectomy
3. Neoplasia
4. Cystic fibrosis
5. Hemochromatosis
6. Fibrocalculous pancreatopathy
7. Others

D. Endocrinopathies
1. Acromegaly
2. Cushing's syndrome
3. Glucagonoma
4. Pheochromocytoma
5. Hyperthyroidism
6. Somatostatinoma
7. Aldosteronoma
8. Others

E. Drug or chemical induced
1. Vacor
2. Pentamidine
3. Nicotinic acid
4. Glucocorticoids
5. Thyroid hormone
6. Diazoxide
7. β-adrenergic agonists
8. Thiazides
9. Dilantin
10. γ-Interferon
11. Others

F. Infections

1. Congenital rubella
2. Cytomegalovirus
3. Others

G. Uncommon forms of immune-mediated diabetes

1. “Stiff-man” syndrome
2. Anti-insulin receptor antibodies
3. Others

H. Other genetic syndromes sometimes associated with diabetes

1. Down syndrome
2. Klinefelter syndrome
3. Turner syndrome
4. Wolfram syndrome
5. Friedreich ataxia
6. Huntington chorea
7. Laurence-Moon-Biedl syndrome
8. Myotonic dystrophy
9. Porphyria
10. Prader-Willi syndrome
11. Others

IV. Gestational diabetes mellitus

Patients with any form of diabetes may require insulin treatment at some stage of their disease. Such use of insulin does not, of itself, classify the patient.

2.2.3.1 Type-I diabetes mellitus

Type-I diabetes characterized by deficiency of insulin due to destructive lesions of pancreatic b-cells; usually progresses to the stage of absolute insulin deficiency. Typically, it occurs in young people with acute-onset with typical symptoms of diabetes together with weight loss and tendency to ketosis, but type 1diabetes may occur at any age, sometimes with slow progression. People, who have antibodies to pancreatic b-cells such as glutamic-acid-decarboxylase (GAD), are likely to develop either typical acute-onset or slow-progressive insulin dependent diabetes. Today antibodies to pancreatic b-cells are considered as a marker of type-I diabetes, although such antibodies are not detectable in all patients.

2.2.3.2 Type-II diabetes mellitus

Type-II diabetes is caused by a combination of decreased insulin secretion and decreased insulin sensitivity. Typically, the early stage of type-II diabetes is characterized by insulin resistance and decreased ability for insulin secretion causing excessive post-prandial hyperglycaemia. This is followed by a gradually deteriorating first-phase insulin response to increased blood glucose concentrations. Type-II diabetes, comprising over 90% of adults with diabetes, typically develops after middle age. The patients are often obese or have been obese in the past and have typically been physically inactive. Ketoacidosis is uncommon, but may occur in the presence of severe infection or severe stress.

2.2.3.3 Gestational diabetes mellitus

Gestational diabetes constitutes any glucose perturbation that develops during pregnancy and disappears after delivery. Long-term follow-up studies, recently reviewed by Kim et al., reveal that most, but not all, women with gestational diabetes do progress to diabetes after pregnancy. In some cases, type-I diabetes may be detected during pregnancy. However women who had diagnosed diabetes before pregnancy cannot be said to have gestational diabetes. The definition applies regardless of the type of treatment needed during the course of the pregnancy and whether the patient remains diabetic after delivery.

2.2.3.4 Other Types

Other types include:

i. Diabetes related to specific single genetic mutations that may lead to rare forms of diabetes, as for instance Maturity Onset Diabetes of the Young (MODY)
ii. Diabetes secondary to other pathological conditions or diseases (as a result of pancreatitis, trauma, or surgery of pancreas)
iii. Drug or chemically induced diabetes.

The clinical classification also comprises different stages of hyperglycaemia, reflecting the natural history of absolute or relative insulin deficiency progressing from normoglycaemia to diabetes. It is not uncommon that a non-diabetic individual may move from one category to another in either direction. Usually, a progression

towards a more severe glucose abnormality takes place with increasing age. This is reflected by the increase in the 2-hPG level with age. The currently valid clinical classification criteria have been issued by WHO and ADA. The WHO recommendations for glucometabolic classification are based on measuring both fasting and 2 hour post prandial glucose (2-hPG) concentrations and recommend that a standardized 75 g OGTT should be performed in the absence of overt hyperglycaemia. The thresholds for diabetes on fasting and 2-hPG values were primarily determined by the values where the prevalence of diabetic retinopathy, which is a specific complication of hyperglycaemia, starts to increase. Even though macrovascular diseases such as CHD and stroke are major causes of death in type-II diabetic patients and people with IGT, macrovascular disease has not been considered in the classification. This sounds illogical and may give an impression that macrovascular diseases are less important than microvascular consequences of diabetes. Classification according to the ADA criteria strongly encourages the single use of fasting glycaemia only without an OGTT.

CRITERIA FOR DIABETIC DIAGNOSIS

ADA Diagnostic Criteria: Normal, Diabetes, and Pre-diabetes

Clinical Practice Recommendations 2010

	Parameter	Normal	Diabetes	Pre-diabetes	Method
1	Fasting Plasma Glucose (mg/dl)	<100	≥126	100–125	No caloric intake for at least 8 h
2	2–h plasma glucose on OGTT (mg/dl)	<140	≥200	140–199	WHO method: 75 g glucose load
3	Random plasma glucose (mg/dl)	<140	≥200	-	with classic symptoms of hyperglycemia or crisis
4	A1C %	<5.7	≥6.5	5.7 – 6.4	NGSP certified method standardized to the DCCT assay

In the absence of unequivocal hyperglycemia, criteria 1, 2, and 4 should be confirmed by repeat testing

2.2.4 Complications of diabetes mellitus

2.2.4.1 Acute Complications

The usual clinical symptoms of DM include polyuria, polydipsia, weight loss, fatigue, weakness, blurred vision, frequent superficial infections, and poor wound healing. However, patients can occasionally present with acute complications, such as hypoglycaemia, diabetic ketoacidosis, hyperosmolar non-ketotic coma.

2.2.4.2 Chronic Complications

The major chronic complications of DM are usually microvascular, neuropathic and macrovascular in nature. The microvascular and neuropathic complications present as retinopathy, nephropathy, peripheral neuropathy, autonomic neuropathy and foot disease. The macrovascular complications present as myocardial infarction/ ischaemia, transient ischaemic attack, stroke and claudication have also indicated that other chronic complications of diabetes may be non-vascular, e.g. gastroparesis, infections and skin changes.

2.2.4.3 Macrovascular Complications

Boyle (2007) stated that in patients with type-II diabetes, there is an increased risk of macrovascular disease. Factors that may play a linkage role in the development of macrovascular disease in type-II diabetes include low concentration of the adipocyte specific protein (adiponectin) , increased production of the vascular cell adhesion molecule-1 and the subsequent adhesion of T-lymphocytes to the endothelial walls of the coronary arteries, higher procoagulation with increased expression of Plasminogen Activator Inhibitor-1 (PAI), and an increased production of Matrix Metalloproteinases (MMPs) by macrophages which ultimately leads to an instability of atherosclerotic plaques. Almdal et al (2004) also indicated that type-II diabetes typically occurs in the setting of the metabolic syndrome, which also includes abdominal obesity, hypertension, hyperlipidaemia, and increased coagulability. These other factors can also act to promote cardiovascular disease. In this setting of multiple risk factors, type-II diabetes itself acts as an independent risk factor for the development of ischemic disease, stroke, and death.

2.2.4.4 Retinopathy

Diabetic retinopathy which occurs in all forms of diabetes is the commonest cause of blindness in adults in most developed countries. The development of retinopathy, as with all diabetic complications, depends on the duration of the disease. The natural history of diabetic retinopathy according to Nathan (1993) has been best defined in IDDM, where it is possible to predict the date of onset of the disease. Course of progression of retinopathy in NIDDM is more difficult to ascertain, since the diabetes may be progressing silently for many years before it is diagnosed. As a result, patients with NIDDM may present with retinopathy and even, rarely, advanced retinopathy at the time of diagnosis. However, the development of retinopathy is still dependent on how long the patient has had NIDDM, as it is in IDDM.

The clinical features of diabetic retinopathy are; 'microaneurysms, retinal haemorrhages, exudates, cotton wool spots, neovascularisation, fibrosis, pre-retinal and vitreous haemorrhages'. These features occur in various combinations in different patients and are used to classify the severity of the disease.

2.2.4.5 Neuropathy

This is a relatively early and common complication affecting approximately half of all patients diagnosed with both types-I and II diabetes. Fauci (2008) asserts that the condition may manifest as polyneuropathy, mononeuropathy, and/or autonomic neuropathy. As with other complications of DM, the development of neuropathy largely depends on duration of diabetes and how well or otherwise glucose levels are controlled. Also increased body mass index and smoking are considered risk factors for developing the complication.

2.2.5 COPD and Diabetes

The term COPD encompasses two other lung diseases, chronic bronchitis and emphysema. COPD is progressive and currently incurable, and without proper diagnosis and treatment, health will continue to deteriorate. With COPD, pulmonary inflammation prevents the proper exchange of air. Diabetes or diabetes mellitus is a term used to describe a group of diseases that affect blood sugar, also known as blood glucose, throughout the body. People with diabetes suffer from high amounts of glucose in the blood, which can lead to numerous health complications and adverse symptoms. The hormone insulin regulates glucose levels.

Two top factors cause COPD to develop–smoking and environmental or occupational pollution. For the most part, diabetes occurs because of genetic and environmental factors. The end result for COPD is that the blood is not properly oxygenated, and for diabetes, low levels of insulin result in skyrocketing glucose in the blood which cannot reach the body's cells to provide energy.

2.2.5.1 The Connection between COPD and Diabetes

Diabetes mellitus (DM) is a common comorbidity of chronic obstructive pulmonary disease (COPD). A series of studies have shown that DM is associated with impaired lung function. The chronic complications of diabetes include a number of pathological changes involving different districts and, among these, lung represents a target organ for diabetic microangiopathy in patients with diabetes. The Framingham Heart Study has reported an association between glycemic status and reduced lung function. The diagnosis of DM was associated with lower adjusted mean residual forced expiratory volume in one second (FEV1) and Forced vital capacity (FVC). The Copenhagen City Heart Study, a longitudinal analysis, has shown an association between a new diagnosis of diabetes and impaired lung function that was more prominent in diabetic subjects treated with insulin compared with subjects treated with oral hypoglycemic agents. In a prospective Australian study, the Fremantle Diabetes Study, 125 patients with type 2 diabetes mellitus (T2D) and no history of lung disease was assessed by spirometry at baseline and revaluated seven years later. The key finding was that the average rate of decline in lung function, as measured by FEV1 was 71 ml/year compared to an expected decline in healthy non-smokers of 25–30 ml/year, suggesting that the exposure to blood glucose may be a strong and consistent negative predictor of lung function follow-up after adjustment for baseline and potential confounders. The association between impaired lung function and diabetes is thought to be the result of biochemical changes in the structures of the lung tissue and airways that involves a series of mechanisms likely due to systemic inflammation, oxidative stress, and hypoxemia or ultimately to the direct damage caused by chronic hyperglycemia. The lung function decline in patients with diabetes may be a consequence of diabetes itself and diabetic patients seem to have an increased risk of several non-neoplastic lung conditions such as asthma and COPD.

2.2.5.2 Epidemiology

Diabetes occurs more often in people with COPD than in the general population, although the exact prevalence varies between studies

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A retrospective analysis examined the relationship between COPD and comorbidities using Health Search Database information obtained from Italian College of General Practitioners that stores information of nearly 1.5 % of the national population. Compared to the non-COPD individuals, COPD patients were at increased risk of DM, 10.5 % in the general population vs. 18.7 % in COPD patients. Unexpectedly, in this study COPD patients had an increased prevalence of both cardiovascular diseases and T2D and a very low prevalence of the metabolic syndrome, suggesting that COPD is a real risk factor for cardiovascular diseases and diabetes,

It has been consistently reported (Table 1) an impaired pulmonary function and glucose intolerance in several cross-sectional and perspective studies. A prospective study conducted in a five years observation period reported that the development of DM was associated with greater rates of decline of pulmonary function suggesting that diabetes may be, in particular at its onset, is associated with a significantly accelerated decline of respiratory function, Lazarus et al within the Normative Aging Study in their perspective analysis reported that FVC was negatively associated with the risk to have higher levels of insulin resistance and a similar associations were found for FEV1 and maximal mid-expiratory flow rate (MMEF), suggesting the possibility that insulin resistance could be the factor correlated with the impairment of pulmonary function. In another prospective study with a median follow up of 13 years, the authors concluded that the risk of developing diabetes is inversely associated with pulmonary function and the longitudinal associations between vital capacity (VC) and diabetes ($P = 0.001$) and log glucose ($P = 0.036$) were significant after adjustments for confounders.

Summary of epidemiological study

COPD risk of T2D	Population studied	Findings
Prospective cohort study with a mean follow up of 20.9 years	n:1,050 men (with no self-reported DM) included in the final analysis mean age: 41.4 years mean BMI: 25.6 kg/m^2	Reduced FVC, FEV_1 and MMEF were associated with greater fasting insulin and fasting insulin resistance after logistic regression analysis.
Prospective cohort study with a mean follow up of 13 years	n: 382 non-diabetic men BMI: 24.4–24.7 years (depends on the pulmonary VC subgroup)	15 new cases of DM 2 were diagnosed during the follow up. DM and glucose were inversely associated with baseline VC.
Prospective cohort study with a follow up of 5 years	n: 9,220 men non-diabetic at baseline mean age: 41.4 years mean baseline BMI: 24.4 $kg/m^2$for patients without type 2 DM at follow up and 26.7 kg/m^2 for patients with type 2 DM at follow up	207 patients developed T2D with the incidence of 2.2 %. FEV1 and FVC were negatively associated with T2D. In patients with BMI < 25 kg/m2 the lowest quartile of FVC and FEV1 had OR of 2.15 (95 % CI 1.02–4.57) and 2.19 (95 % CI 1.09–4.42) for incident T2D.
Prospective cohort study. From 1988 to 1996	data from the Nurses' Health Study from 1988 to 1996 which enrolled 103,614 females	COPD was found to have a multivariate RR of 1.8 (95 % CI 1.1-2.8) for new onset T2D.
Prospective study of middle-aged and older US women followed over 12 years	38,570 women who were aged ≥ 45 years, free of cardiovascular disease and cancer at baselineand free of diabetes at baseline	The presence of COPD was associated with an approximately 1.50-fold increased risk of T2D independently of traditional diabetes risk factors including cigarette smoking

COPD risk of T2D	Population studied	Findings
Cohort from the Genetic Epidemiology of COPD Study (COPDGene)	smokers with and without COPD at 21 clinical centers throughout the United States Between 2007– 2011	Non-emphysematous COPD, defined by airflow obstruction with a paucity of emphysema on chest CT scan, is associated with an increased risk of diabetes.

The Nurses' Health Study, a prospective cohort study, during the 8 years follow-up found that the risk to have T2D was significantly higher in patients with COPD than those without COPD (multivariate relative risk 1.8, 95 % CI 1.1–2.8) nor those with asthma. These data suggest that COPD could be a risk factor for developing T2D, perhaps sharing common inflammatory and cytokine profile. In another Korean study, planned to assess the relationship between lung function and incident T2D, 9,220 men without T2D were prospectively followed for five years. The authors found that impaired lung function is independently associated with the incidence of T2D. FVC and FEV1 were negatively associated with T2D ($P < 0.05$) independently by confounding factors. It is therefore proposed on the basis of these results, the possibility that the reduced lung function, as measured by FEV1 and FVC, may precede the development of T2D.

Differently, in a prospective study conducted in a cohort of 38,570 women with median follow-up of 12.2 years, the hypothesis that asthma or COPD could be involved in the pathogenesis of T2D was tested. Both asthma and COPD were individually and independently associated with an increased risk of T2D in women; this association was independent of cigarette smoking and other diabetes risk factors and also persisted after excluding all COPD cases with asthmatic symptoms. The multivariate RRs were 1.38 (95 % CI, 1.14–1.67) for COPD without asthmatic symptoms. Recently, an increased prevalence of diabetes in non-emphysematous COPD patients (diabetes OR 2.13, $p < 0.0001$) has been reported in the COPD Gene Study, where patients were classified in emphysema-predominant and non-emphysematous COPD based on CT scan features. Although comorbidities were self-reported, previous studies have shown that it is a reliable source of information. This

association persisted also after performing stratified analyses considering obese and non-obese individuals, smoking habit, obstruction severity divided in GOLD 1– 2 and GOLD 3– 4, ethnicity and age. These results were also confirmed by the ECLIPSE study, where diabetes was reported in 10.6 % of non-emphysema and in 8.2 % of emphysema-predominant COPD. The authors suggested to evaluate for diabetes patients with COPD, especially those defined non-emphysema.

In a study conducted in UK using the wide primary care data to quantify the burden of comorbidity among individuals with COPD, it has been shown that COPD is associated with an increased odds of DM. Intriguingly the effect of COPD having DM is higher in current smokers for the younger patients, but after the age of 45 becomes greater in non-smokers, suggesting that this association was independent of smoking status.

2.2.5.3 Mechanisms

DM is a common comorbidity of COPD. What are the mechanisms underlying the increased prevalence of diabetes in COPD still remains unclear, although a number of potential pathways including inflammation, oxidative stress, hypoxia and chronic hyperglycemia may provide some explanation.

Systemic inflammation is a common feature to both COPD and to T2D, which drives insulin resistance, atherosclerosis and many systemic expressions of COPD itself. The presence of systemic inflammation is poorly defined in patients with COPD. Most of the studies were cross-sectional and show that not all patients with COPD have a systemic inflammatory response. However systemic inflammation is a risk factor for the development of many chronic diseases, which are COPD co-morbidity. However, we should consider that the persistent systemic inflammation in COPD patients is associated with significantly worse outcomes in terms of mortality and exacerbation rate as demonstrated by the ECLIPSE study. It appears to be mostly independent from the pulmonary component of the disease, raising the possibility that systemic inflammation could be a possible therapeutic target in these patients. The possible development of COPD and T2D could have evidence in the context of a chronic systemic inflammation with the presence of cardiovascular disease or metabolic disorders, known to be related to systemic inflammation, increasing the

association between COPD and DM. In any case, systemic inflammation might be increased by the coexistence of these two conditions, COPD and diabetes, worsening both in their clinical manifestations.

There are many evidences that the levels of inflammatory proteins (Table 2), such as cytokines and among these TNF- α, IL-6, or C reactive protein (CRP), are increased in patients with COPD. Systemic inflammation is associated with various complications in COPD, including cardiovascular and metabolic diseases such as diabetes.

Potential mediators involved in the higher prevalence of T2D in COPD

	COPD	**DM**
CRP	COPD is independently associated with increased levels of CRP. Moreover, CRP may predict the future onset of COPD.	Elevated CRP levels may predict the development of onset of T2D.
TNF-α	COPD is independently associated with increased levels of TNF-α. activates NF-kB leading to cytokine production, upregulation of adhesion molecules and increasing oxidative stress	May be a risk factor for the development of new onset T2D. May interfere with glucose metabolism and insulin sensitivity, and can be antagonized by adiponectin which reduces NfkB activation.
IL-1	IL-1 is implicated in the pathogenesis of COPD related inflammation.	An increase in IL-1β may predict the development of new onset T2D.

	COPD	DM
IL-6	COPD is independently associated with increased levels of IL-6. This cytokine is a potent stimulator of CRP production by the liver and may account for the increase in circulating CRP found in patients with COPD.	IL-6 was shown to increase the risk for the new onset T2D.
Leptin	Leptin levels are increased in patients with COPD. May contribute to COPD related weight loss, PFT decline and prolonged hospital stay. Leptin induced IR and hyperglycemia	Leptin may increase the risk of T2D. Leptin may participate in the development of DM related complications via its proinflammatory actions.
Adiponectin	Adiponectin levels are increased in patients with COPD and low BMI, Increased adiponectin was related to a decrease in cardiovascular mortality, but was associated with an increase in mortality due to respiratory causes.	Adiponectin may prevent the development of T2D via its anti-inflammatory and proinsulin actions.
Resistin	Resistin levels may be increased in COPD and mediate IR.	Resistin may directly participate in the development of IR
Catecholamine	Patients with COPD had higher catecholamine levels which were independently related to a decrease in FEV1.	Insulin antagonists and contribute to the occurrence of hyperglycemia. Abnormalities in the renin angiotensin aldosterone system (RAAS) are implicated in the development and pathogenesis of cardiovascular diseases, Metabolic Syndrome and T2D

	COPD	DM
NF-kB	NF-kB activation is implicated in systemic inflammation and could be involved in skeletal muscle dysfunction in COPD patients	NF-kB activation has also been associated with Diabetes

TNF-α is a marker of systemic inflammation that appears to be associated with the severity of COPD, increased levels are seen in severe and very severe COPD. On the other hand, high levels of TNF- α may be a risk factor for the development of new-onset T2D, interfering with glucose metabolism and insulin sensitivity, suggesting a possible link between COPD and T2D.

Oxidative stress is generated by an imbalance between oxidants and antioxidants. In COPD patients, either in stable or during acute exacerbations, oxidative stress is increased mainly by inhalation of oxidants such as those generated by cigarette smoke or pollution, or as a result of inflammatory leukocytes that are activated to release reactive oxygen species. This condition can cause direct damage to the lung targeting lipids and proteins, triggering specific pathways, which could generate increased gene expression, production pro-inflammatory cytokines and ultimately increased inflammation. Finally adiponectin, an adipokin with intrinsic anti-inflammatory property, correlates with COPD; data obtained in case-control studies demonstrated a higher systemic and airway adiponectin concentrations in COPD patients mainly men than controls. Moreover serum adiponectin has a positive correlation with lung function in healthy adults, whereas an inverse correlation has been found in studies conducted in male individuals with COPD.

In T2D oxidative stress is present through the activation of specific biochemical pathways, increased production of reactive oxygen species, and reduction of antioxidants and furthermore increase lipid peroxidation. Oxidative stress, mainly smoke-induced in COPD patients, could cause in T2D the continuation of the insulin resistance by altering the production of energy. Conversely oxidative stress produced by T2D might worsen COPD activating inflammation and even compromising the response to glucocorticoids.

Smoking induces oxidative stress that can trigger local and systemic inflammation, though cigarette smoking is not a link between DM and COPD. This is especially interesting given that exposure to cigarette smoking is crucial for the development of COPD and, at the same time, an independent and modifiable factor for the development of DM. Since cigarette smoking does not appear to be the connection, it is likely that other mechanisms besides systemic inflammation or oxidative stress could define the link between DM and COPD.

Current evidence suggests that COPD, in which hypoxia is one of the typical features, is associated with increased levels of oxidative stress, but likewise an excessive oxidative stress may be a risk factor for new-onset T2D it can be also a result of new onset DM. Moreover, the induction of increased levels of reactive oxygen species (ROS), NF-kB and intracellular mediators of inflammation could also lead to chronic hyperglycemia and to an increased synthesis of collagen mediated by higher levels of advanced glycation end products that ultimately would affect negatively lung function.

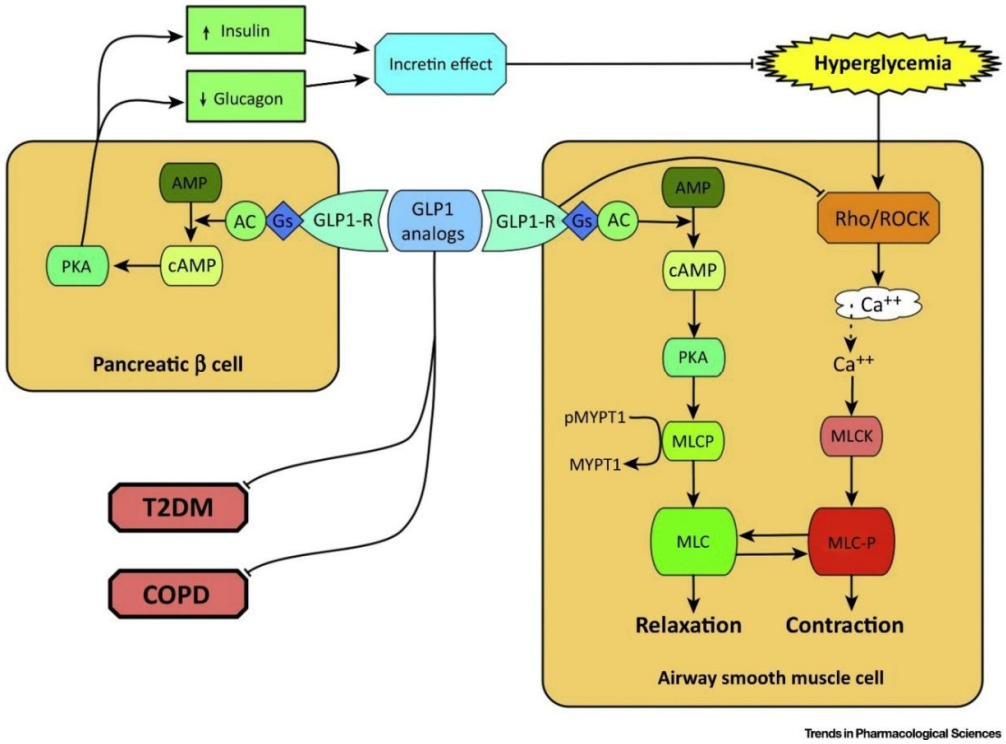
Hypoxia causes significant changes in metabolism, studies conducted in healthy subjects at high altitude showed increased insulin resistance and glucose production in the liver with greater insulin sensitivity at peripheral level and increased uptake of glucose in skeletal. It seems that pancreatic β cells are sensitive to hypoxia-induced damage, regardless of the condition of intermittent hypoxia as that observed in sleep apnea, or chronic hypoxia seen in COPD. Indeed, chronic hypoxia has been observed in association with impaired glucose tolerance, reduced insulin sensitivity accompanied by greater lipolysis. In COPD patients, in which the normalization of saturation values has been obtained, it can be observed an improvements of glucose tolerance and insulin sensitivity. It is possible that both of these diseases, COPD and DM, might share common pathophysiological pathways which can be mediated by hypoxia inducible factor (HIF).

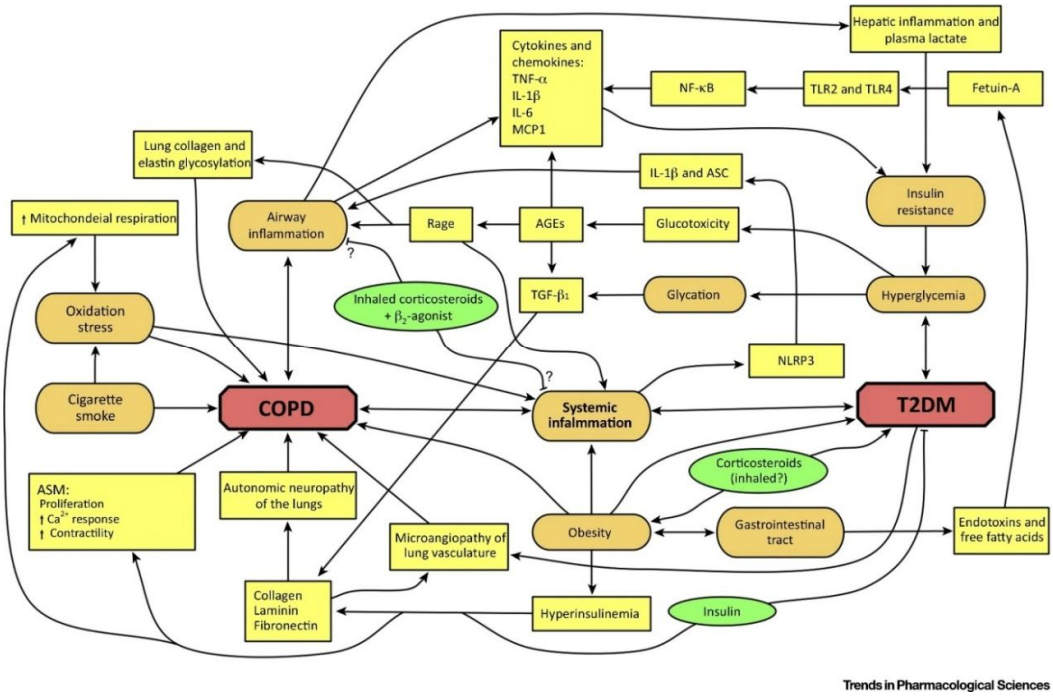
Inflammation, oxidative stress and hyperglycemia in particular, have been shown to induce muscle dysfunction. Lower lung function has also been suggested to be associated with increased serum osmolarity, where blood sugar contributes to the

total serum osmolarity. A number of prospective studies have shown that reduced lung function is an independent predictor of T2D. In particular, in a prospective study on lung function in adults with T2D, it has been suggested the idea that alterations in lung function may precede diabetes and then will progress after the onset of diabetes itself.

The data suggested that the glucose-induced enhancement of bronchial responsiveness is likely to be due to increased activation of a particular intracellular pathway: the Rho-kinase pathway. It seems that the Rho/ROCK pathway plays a role in regulating several biological pathways, including some that affect the level of airway smooth muscle (ASM) tone. The activation of this pathway mediates multiple biological functions involving contractility based on actin-myosin. Moreover, our results suggested that the Rho/ROCK pathway, together with the mobilization of the intracellular calcium and the phosphorylation of MYPT-1, might play a crucial role in the reduced lung function observed in patients with diabetes. It is widely accepted that airway hyper responsiveness is a risk factor for an accelerated decline in FEV1 and the development of obstructive pulmonary disease such as COPD. As well as pulmonary function impairment that is greater in patients with poorly controlled diabetes, a finding that, however, is not explained by obesity or increasing age.

2.2.5.4 Targeting Mechanisms Linking COPD to Type II Diabetes Mellitus





2.2.6 Glycated Haemoglobin (HbA1C)

HbA1c was introduced into clinical use in the 1980s and subsequently has become a cornerstone of clinical practice. HbA1C reflects average plasma glucose over the previous eight to 12 weeks.It can be performed at any time of the day and does not require any special preparation such as fasting. These properties have made it the preferred test for assessing glycaemic control in people with diabetes. More recently, there has been substantial interest in using it as a diagnostic test for diabetes and as a screening test for persons at high risk of diabetes.

In 2009, The International Expert Committee recommended the use of HbA1C to diagnose diabetes mellitus with a threshold > 6.5%. However, the diagnosis should be confirmed by a repeat test unless symptoms of hyperglycaemia and blood glucose level of >11.1 mmol/l (>200mg/dl) are available.In addition, those with an HbA1C level between 6 and 6.5% have been identified as being at very high risk of developing diabetes, and the risk increases substantially as the values increase.

The ADA's recommended goal for HbA1C is <7% in all patients with diabetes mellitus. The same level is recommended for primary prevention of cardiovascular disease in people with diabetes. The ideal HbA1C goal for individual diabetic patients is as low as <6% without causing significant hypoglycaemia. The recommendations are the same for T1DM and T2DM. The ADA recommends checking HbA1C levels at least twice a year in patients with relatively stable glycaemic control and quarterly among those whose HbA1C targets are not achieved, particularly if drugs are changed, to determine the effect of such changes.

HbA1C and CHD in Patients with Diabetes

Diabetes patients face an 11% increased risk of mortality from ischaemic heart disease. While those with HbA1C >8% face a 150% increased risk of death from heart disease. Cardiovascular complications are usually present at the diagnosis of T2DM, because diabetes is preceded by long period of asymptomatic hyperglycaemia, called impaired glucose tolerance. Classical CV risk factors such as smoking, hypertension, and hypercholesterolemia do not account for the excess risk of CV morbidity and mortality in patients with elevated HbA1C levels. This association is equally important in both T1DM and T2DM, and exists across ethnic and geographical boundaries.

Materials and Methods

CHAPTER-III

MATERIALS AND METHODS

3.1 STUDY AREA AND SETTING

The study covered the period of April 2016 to July 2018 at the Govt. Siddha Medical College and Hospital, Palayamkottai- 627 002, Tirunelveli, Tamil Nadu. All procedures were approved by the IEC, DR MGR Medical University, Chennai.

3.2 STUDY DESIGN

An open labelled randomized clinical trial of 40 type-II diabetic patients. The participants were newly diagnosed and already diagnosed as type-II diabetics and undergoing treatment. A written informed consent form was completed by all the participants who were recruited into the study. The purpose of the study was explained to the participants in local language they understand. Proformas were used to record information of the participants. Information on demography, life style, anthropometric measurements and Siddha parameters were taken.

40 patients of both sexes of 40 to 75 age groups were recruited for study and treated with the trail drug till the end of the study period of 90 days. Of the 40 patients, 20 were treated as in patients. After discharge, the IP cases were followed in OP until the completion of the study.

Study type **:** A Prospective Open labelled Randomized Clinical trial.
Study Place **:** Govt. Siddha Medical College and Hospital, Palayamkottai - 627002
Study Period **:** 24 months.
Sample size **:** 40 patients

3.3 SELECTION OF PATIENTS

The inclusion of cases in the study was based on the screening of patients with Iya Neerizhivu. The criteria for screening were increased fasting, post prandial sugar levels along with high level of HbA1C, Spirometry test & Dyspnea Scale Score.

Detailed personal history, family history, occupation, habits, clinical symptoms, medical history, and the duration of illness were recorded for each and every patient (Proforma annexed).

3.3.1 INCLUSION CRITERIA

1. Age between ≥ 40 and ≤ 75 years
2. Type II diabetes mellitus, previously diagnosed diabetic patients which are uncontrolled or poorly controlled for more than 5 years duration of the illness.
3. If yes in any of three
    a. FBS - > 126 mg/dl and ≤250mg/dl or
    b. PPBS - > 200mg/dl and ≤350mg /dl or
    c. HbA1c > 6.5 and<12
4. Patient with respiratory complaints such as, Coughing, sputum and Dyspnea
    a. FEV_1/ FVC <0.70 and FEV1 <80%
    b. MMRC Dyspnea score ≥2
5. Willing to give blood sample for the investigations
6. Patients who are mono therapy alone

3.3.2 EXCLUSION CRITERIA

1. Age below <40 years and >75 years
2. History of occupational exposure
3. Participation of pulmonary rehabilitation program with 12 months
4. Systemic hypertension, angina, heart failure
5. Any physical disability that may affect lung function as kyphoscoliosis, pectus excavatum and pectus carinatum.
6. Resting O_2 saturation < 90%
7. Type 1 diabetes mellitus
8. Pregnancy
9. Lactating mother
10. Chronic kidney disease / Renal failure
11. Prolonged Corticosteroid therapy
12. Chronic active viral hepatitis/cirrhosis/ascites
13. Auto Immune disorder

WITHDRAWAL CRITERIA: The investigator shall withdraw the patients from the study if,

1. FBS rises to >200mg/dl or PPBS level increases to >350mg/dl or respiratory complaints are not controllable within fifteen days
2. Shortness of breath from COPD resulting in the patient too breathless to leave the house, or breathless after dressing or undressing or the presence of chronic respiratory failure or clinical signs of right heart failure and FEV1 30% - 39% predicted FEV1 / FVC < 0.7
3. Any serious complication develops, which required urgent treatment with any other Drug/ therapy
4. Patients turned unwilling to continue in the course of clinical trial

The investigator will mention the probable course of withdrawal and provide possible medical treatment to manage the illness.

3.3.3 DIAGNOSIS

The Siddha parameters of diagnosis of diseases were implemented in the inclusion of cases for the study which are,

- Poriyal Arithal
- Pulanal Arithal
- Vinathal
- Mukkutra nilaigal
- Envagai thervugal
- Nilam
- Kaalam & Udal kattugal

3.3.4 INVESTIGATIONS

1. **Blood:**
    a. HBA_1C, FBS, RBS, PPBS
    b. Lipid profile
    c. CRP

2. **Sputum Examination**
    a. AFB
    b. Culture suitable in selected cases
3. **Pulmonary function tests (computerized Spirometric tests)**
    a. FVC - forced vital capacity
    b. FEV_1- forced expiratory volume in one second
    c. MMEF – Maximum mid expiratory flow
    d. PEFR- Peak expiratory flow rate (By peak flow meter)
4. **Chest X-ray**
    a. PA View
5. **BMI**

2. Urine:

- Albumin, Sugar, Deposits

The Biochemical Analysis was carried out before and after treatment at the time of discharge, along with regular blood sugar monitoring once in twenty days.

3.4 TREATMENT

The trial medicine choosen for the clinical study was **Seenthil Sarkkarai** 30 mg/Kg/BW/daily three times a day it was titrated considering the BMI of the patient and dose adjusted accordingly.

Trial Medicine	: ***Seenthil Sarkkarai***
Reference	: ***Gunapadam (Mooligai Vaguppu) C.S.Murugesu Mudaliyar***
Dosage	: **30 mg/ Kg/BW/daily three times a day**
Adjuvant	: **Ghee**
Duration	: 9**0 days**

3.4.1 Preparation of Trial Medicine

Purification and Preparation of Seenthil Sarkkarai

All the ingredients of these herbal formulations will purify according to the suitable procedure methods described in Siddha classical literature. Cut and remove the outer covering of aged stem of Tinospora cordifolia will be shade dried and make into powder. Add 1400 ml water and knead well, then mix 5600ml water and allow precipitating. The flour of Tinospora Cordifolia will be precipitated in the latter. After filter the water and again add 5600 ml water into it and allow to precipitating. It will be done for 10 times. Then add kaadi neer mixed with lemon juice (16:1) allow to precipitating for one day. Like another day buttermilk and lemon juice (16:1) allow to precipitating. The ratio should be maintained to flour and solution is 1:4. Finally flour will be collected and dried.

Drug Storage

The trial drug is stored in clean dry air tight container and it is dispensed to the patients in packets

3.4.2 Collection and authentication of Trial Medicine

The stems of Tinospora cordifolia (climber) will be freshly collected from in and around the areas of Palayamkottai and Thirunrlveli, Tamilnadu. The plant will be identified and authenticated by the Medicinal Botanist and Gunapadam experts at Government Siddha Medical College and Hospital, Palayamkottai - 627002. The specimen sample of all the herbs will be preserved in PG Gunapadam department individually for future reference

3.4.3 Preclinical Analysis of Trial Medicine

All the preclinical studies of the drugs which had included Bio chemical and pharmacological studies had done and cross checked before beginning the trial. The Biochemical analysis had done in Dept. of Biochemistry, GSMCH, Palyamkottai.

All the preclinical studies of the drugs which include Physical, Biochemical and Pharmacological studies will be done and will be cross checked before beginning the trial.

3.4.4 Ethical Review

The trial was conducted in accordance with the ethical principles that are consistent with Good Clinical Practice guidelines and obtained prior approvals before start of the trial from the Institutional Ethics Committee of GSMCH, Palayamkottai (No: GSMC/3-IEC/2016-I-6/20.07.2016 Dated 20.07.2016) and Institutional animal ethical committee (IEAC) of K.M. College of Pharmacy, Madurai (TNMGRMU/KMCP/IEAC/312). The trial was applied and approved in Clinical Trial Registry of India.

3.4.5 Study Enrolment

Participants were informed in Tamil language, regarding the trial, the expected benefits and their right to opt-out of trial at any time without prejudice. Informed written consent was obtained from each participant, prior to his/her inclusion into the trial.

Type II Diabetes Patient reporting at the OPD with the clinical features sustained with dyspnea, coughing and sputum are chosen for enrolment based on the inclusion criteria. The patients who are enrolled are informed about the study trial drug, possible outcomes and the objectives of the study in the language and terms understandable to them and the informed consent would be obtained in writing from them in the consent form

Before commencing the trial all the subjects were advised diet based on their body mass index, but no recommendations on diet were given during trial period. All subjects of age range between 40-70 years with Fasting Plasma Glucose (FPG) >110mg/dl and two-hour Postprandial Plasma Glucose (PPPG) between >160mg/dl and with a. FEV1/ FVC <0.70 and FEV1 <80%, MMRC Dyspnea score ≥2 were included in the study.

The subjects with history of serious adverse effects or hypersensitivity reactions to the medication such as rashes, diarrhoea, vomiting etc., and history of treatment with other anti-hyperglycaemic drugs, active liver disease or hepatic dysfunctions, higher serum creatinine (> 2.5 mg/dl) and serious or unstable medical or psychological condition are excluded from the study.

During each visit, body weight, blood pressure, respiratory system and cardiovascular were examined clinically. During each visit adverse effects present if any were documented.

At the end of the study period, all the patients were instructed to follow diet control, regular exercise, Pranayamam, yoga, meditation and to monitor their blood sugar levels, HbA1C, and lipid levels periodically. They were also advised to pursue the further treatment in the PG, Pothu Maruthuvam OP for the follow up study.

3.4.6 Statistical Analysis

All data were analysed using the SPSS 25.0 (IBM). Data were expressed as means and standard deviation. The significance of the difference between the means of the baseline and the final examinations was tested using the paired “t” test. A probability value of <0.05 was considered to be statistically significant.

Result and Observation

CHAPTER-IV
RESULTS AND OBSERVATIONS

PREFACE

This study was a hospital based an A Prospective Open Labelled Randomized Phase II Clinical Trial of "SEENTHIL SARKKARAI" for IYA NEERIZHIVU (Chronic Obstructive Pulmonary Disease in Type II Diabetes Mellitus) and evaluates blood glucose level and pulmonary function in type-II diabetic subjects. In addition to assessed healthcare standards, patient's knowledge and Siddha parameters were among diabetic patients. To perform this, analysis was done to see if there is any difference in patients. An attempt was done to correlate between all parameters. The results of this study covered 40 known diabetic type-II patients. All patients were under the treatment for COPD in diabetes type-II. Plasma glucose level (FBS and PPBS) and Pulmanoray Function Test, MMIR score, Serum lipid profile (total cholesterol (TC), triglyceride (TG), Low-density lipoprotein cholesterol (LDL-C), High-density lipoprotein cholesterol (HDL-C) and Very low-density lipoprotein cholesterol (VLDL-C) were measured.

The results were observed with respect to the following criteria by clinical study on 20 out patients and 20 In patients of both sexes. The criteria were.

1. Distribution of Gender
2. Distribution of Age
3. Distribution of Educational
4. Distribution of Occupation
5. Distribution of Religion
6. Distribution of Marital Status
7. Distribution of Clinical Manifestation
8. Distribution of Mode of Onset
9. Distribution of Duration of Illness
10. Distribution of Family History
11. Distribution of History of Previous Treatment of Madhumegam
12. Distribution of Personal History

13. Distribution of Socio-Economical Status
14. Distribution of Other System Involvement
15. Distribution of Body Mass Index
16. Distribution of Constitution of Body
17. Distribution of Gunam
18. Distribution of Kaalam
19. Distribution of Paruva Kaalam
20. Distribution of Thinai
21. Distribution of Mukkutram
    a). Derangement of Vatham
    b). Derangement of Pitham
    c). Derangement of Kapham
22. Distribution of Involvement of Udal Thathukkal
23. Distribution of Kanmenthiriyam
24. Distribution of Imporigal (Gnanendrium)
25. Distribution of Kosam
26. Distribution of Conditions of Envagai Thervugal
27. Distribution of Neer Kuri
28. Distribution of Nei Kuri
29. Distribution of Laboratory Analysis
    a). HbA1C
    b). Blood Glucose
    c). PFT
30. a). Changes in HbA1C, Blood Sugar and PFT before and after treatment
    b). Changes in Body Mass Index
    c). Gradation of Results

1.DISTRIBUTION OF GENDER

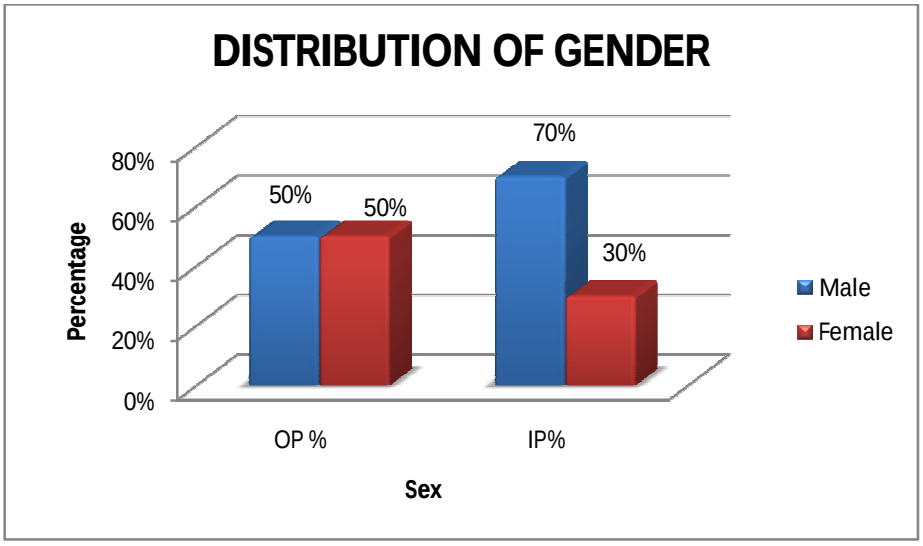
Table-1 illustrates the distribution of sex and its percentage.

TABLE-1

DISTRIBUTION OF GENDER

Sl. No.	Sex	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Male	10	50%	14	70%
2.	Female	10	50%	6	30%
Total		**20**	**100%**	**20**	**100%**

FIGURE-1



In 40 patients included in the study Iya Neerizhivu is distributed in both sexes. Table shows among 20 OP patients 50% were female and 50% were male, among 20 IP patients 70% were male 30% were female.

2.DISTRIBUTION OF AGE

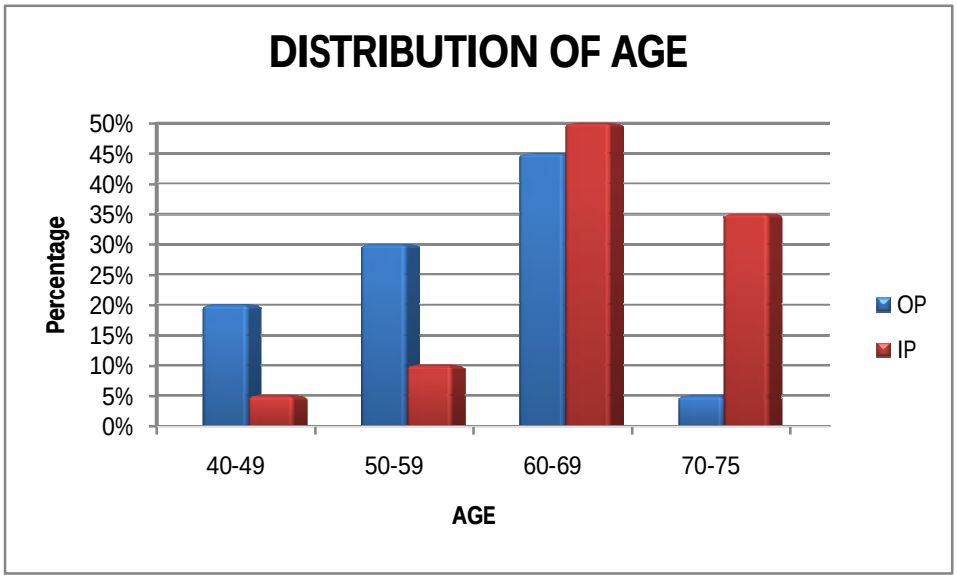
Table-2 illustrates the distribution of age and its percentage.

TABLE-2

DISTRIBUTION OF AGE

Sl. No.	Age group (In years)	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	40-49	4	20%	1	5%
2.	50-59	6	30%	2	10%
3.	60-69	9	45%	10	50%
4.	70-75	1	5%	7	35%
Total		**20**	**100%**	**20**	**100%**

FIGURE-2



The highest incidence was in Iya Neerizhivu. Among the 20 OP and 20 IP patients observed 45% and 50% were affected in age group of 60-69 years, age group of 70-75 closely followed and given among 20 patients in OP 5% were affected and among 20 patients in IP 35% were affected.

3.DISTRIBUTION OF EDUCATIONAL STATUS

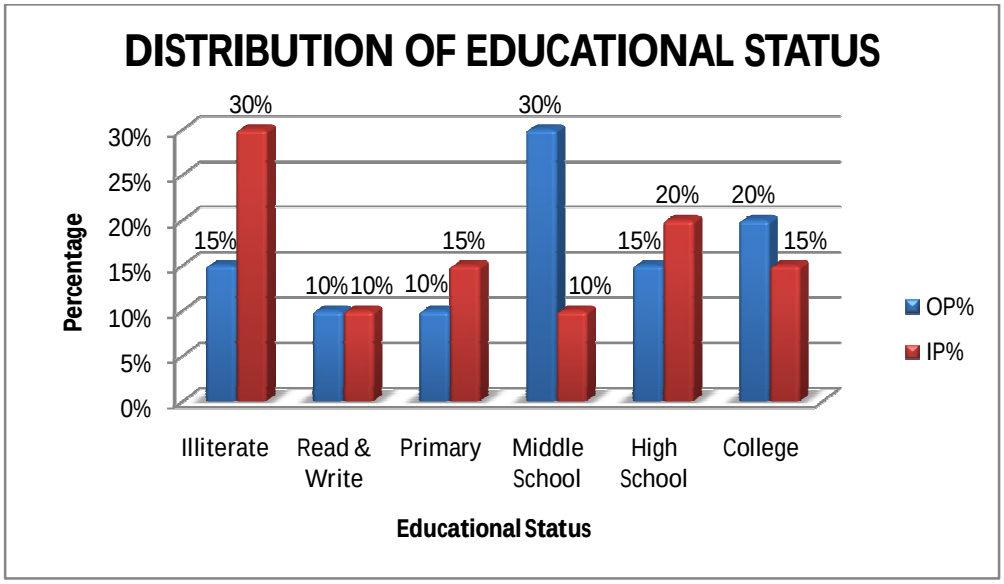
Table-3 illustrates the distribution of Educational and its percentage.

TABLE-3

DISTRIBUTION OF EDUCATIONAL STATUS

Sl. No.	Educational Status	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Illiterate	3	15%	6	30%
2.	Read & Write	2	10%	2	10%
3.	Primary	2	10%	3	15%
4.	Middle School	6	30%	2	10%
5.	High School	3	15%	4	20%
6.	College	4	20%	3	15%
Total		**20**	**100%**	**20**	**100%**

FIGURE-3



From the above table, it is observed that highest incidence of Iya Neerizhivu among 20 out patients was attended High School with 15% and among 20 in patients was attended College school with 20%.

4.DISTRIBUTION OF OCCUPATION

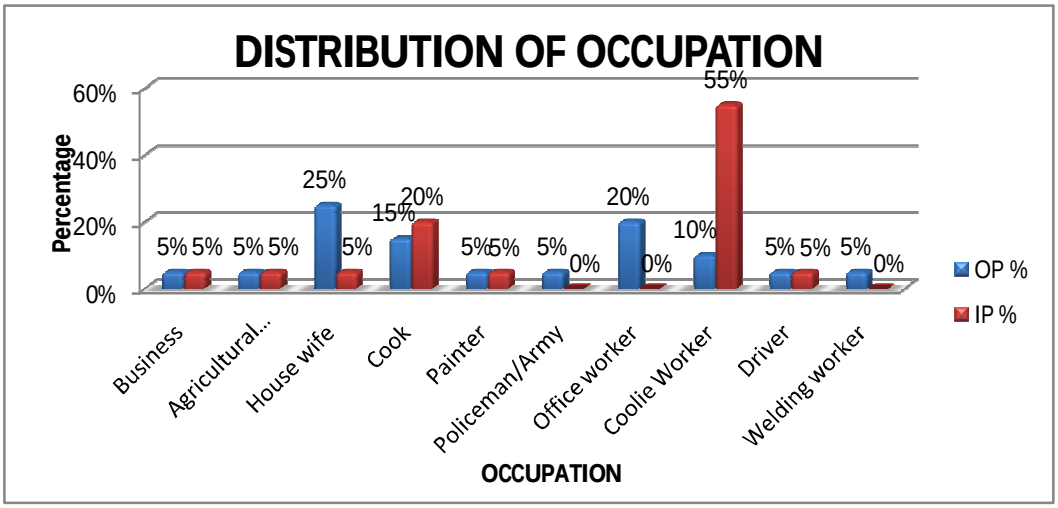
Table-4 illustrates the occupation and its percentage.

TABLE-4

DISTRIBUTION OF OCCUPATION

Sl. No.	Occupation	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Business	1	5%	1	5%
2.	Agricultural Labours	1	5%	1	5%
3.	House wife	5	25%	1	5%
4.	Cook	3	15%	4	20%
5.	Painter	1	5%	1	5%
6.	Policeman/Army	1	5%	-	-
7.	Office worker	4	20%	-	-
8.	Coolie Worker	2	10%	11	55%
9.	Driver	1	5%	1	5
10.	Welding worker	1	5%	-	-
	Total	**20**	**100%**	**20**	**100%**

FIGURE-4



Population employed in various occupations have observed the highest incidence of IyaNeerizhivu. 25% OP patients were house wives 55% IP patients were Coolie Worker.

5.DISTRIBUTION OF RELIGION

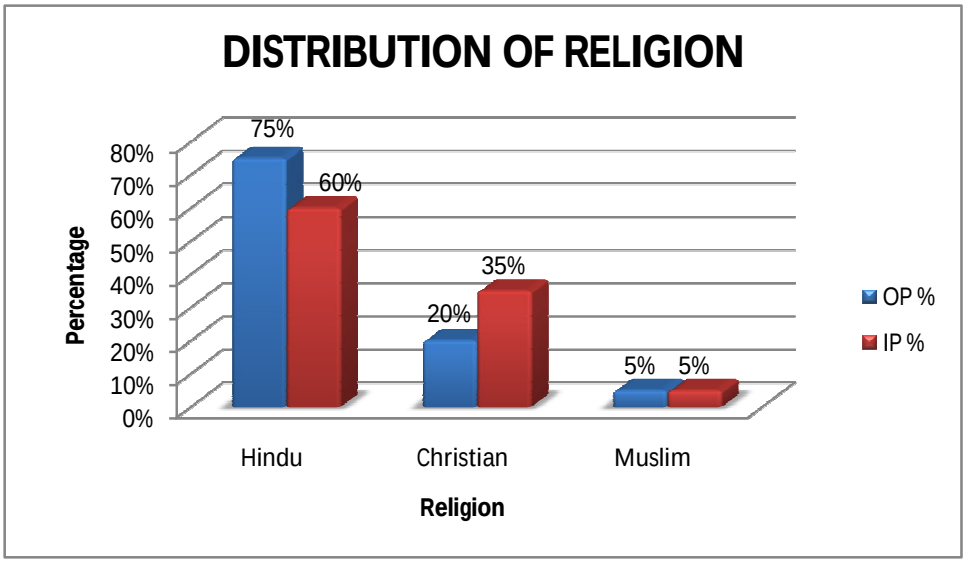
Table-5 illustrates the distribution of religion and its percentage.

TABLE-5

DISTRIBUTION OF RELIGION

Sl. No.	Religion	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Hindu	15	75%	12	60%
2.	Christian	4	20%	7	35%
3.	Muslim	1	5%	1	5%
Total		**20**	**100%**	**20**	**100%**

FIGURE-5



From the above table, it is observed that among 20 out patients 75% were Hindus, 20% were Christians and 5% were Muslims, among 20 in patients 60% were Hindus and 5% were Muslims.

6.DISTRIBUTION OF MARITAL STATUS

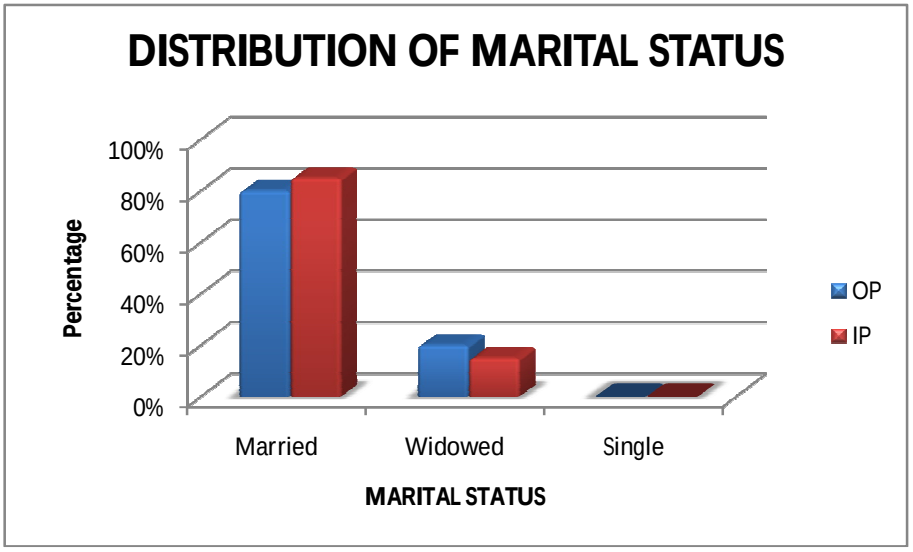
Table-6 illustrates the distribution of religion and its percentage.

TABLE-6

DISTRIBUTION OF MARITAL STATUS

Sl. No.	Marital Status	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Married	16	80%	17	85%
2.	Widowed	4	20%	3	15%
3.	Bachelor	-	-	-	-
Total		**20**	**100%**	**20**	**100%**

FIGURE-6



The highest incidence among the OP and IP patients were married 80% and 85%. Widowed among both OP and IP were 20% and 15%.

7. DISTRIBUTION OF CLINICAL MANIFESTATION

Table-7 illustrates the clinical manifestation and its percentage.

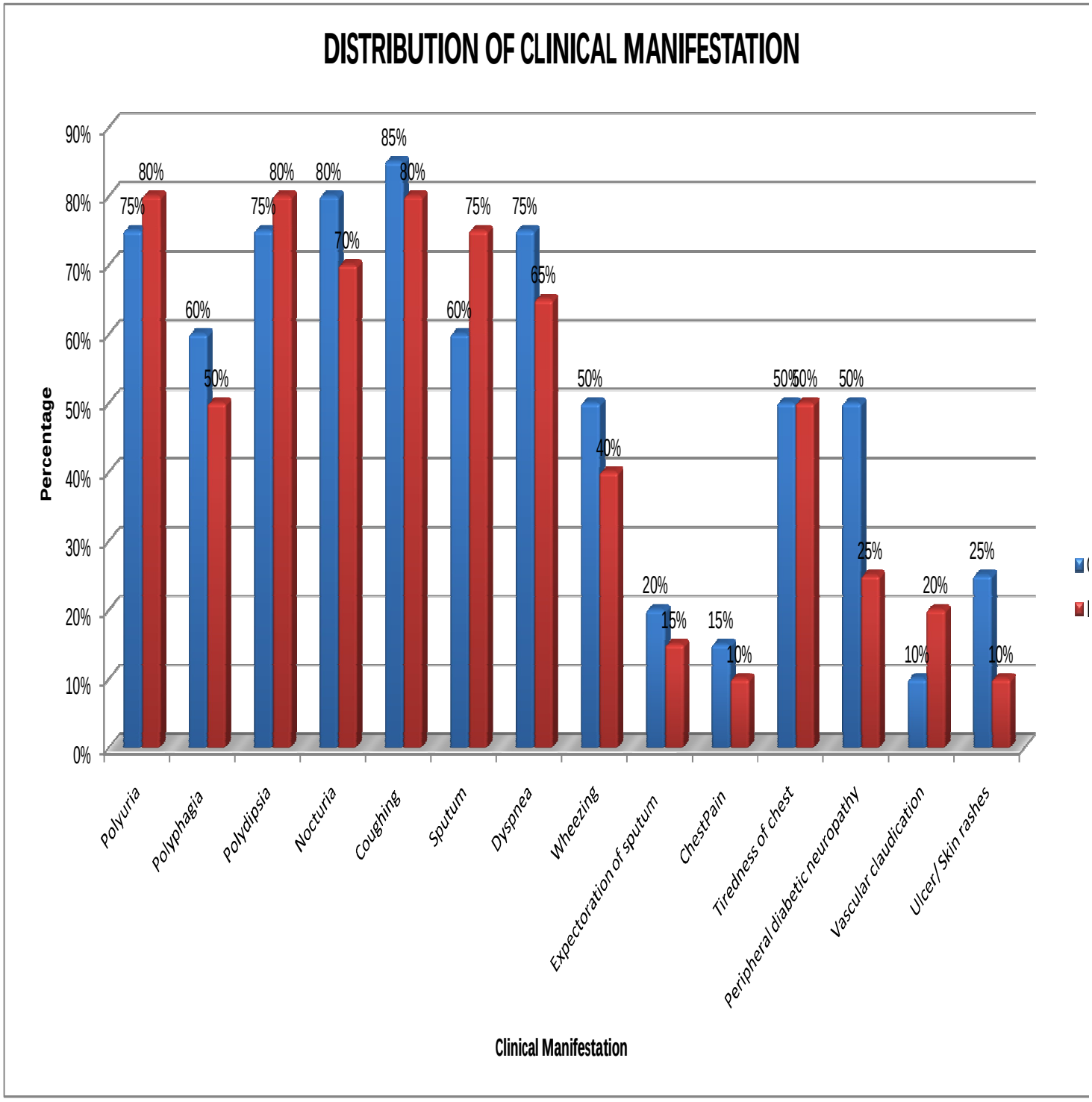
TABLE-7

DISTRIBUTION OF CLINICAL MANIFESTATION

Sl. No.	Clinical Manifestation	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Polyuria	15	75%	16	80%
2.	Polyphagia	12	60%	10	50%
3.	Polydipsia	15	75%	16	80%
4.	Nocturia	16	80%	14	70%
5.	Coughing	17	85%	16	80%
6.	Sputum	14	60%	15	75%
7.	Dyspnea	15	75%	13	65%
8.	Wheezing	10	50%	8	40%
9.	Expectoration of sputum	4	20%	3	15%
10.	ChestPain	3	15%	2	10%
11.	Tiredness of chest	10	50%	10	50%
12.	Peripheral diabetic neuropathy	10	50%	5	25%
13.	Vascular claudication	2	10%	4	20%
14	Ulcer/ Skin rashes	5	25%	2	10%

From the above table, it is observed that among 20 out patients 75% of cases had polyuria and polydipsia and 50% had tiredness. 75% dyspnea, 80% nocturia, 60% had polyphagia, 50% had peripheral diabetic neuropathy, Coughing 85% had skin rashes, 25% had visual impairment, and 60% had Sputum .Among 20 In patients 80% of cases had polyuria polydipsia and 50% had tiredness. 90% had pain, 70% nocturia, 50% had polyphagia, 25% had peripheral diabetic neuropathy, 65% had dyspnea, 15% had Expectoration of sputum visual impairment.

FIGURE-7


DISTRIBUTION OF CLINICAL MANIFESTATION
Percentage
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
75%
80%
60%
50%
75%
80%
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10%
Polyuria
Polyphagia
Polydipsia
Nocturia
Coughing
Sputum
Dyspnea
Wheezing
Expectoration of sputum
ChestPain
Tiredness of chest
Peripheral diabetic neuropathy
Vascular claudication
Ulcer/ Skin rashes
Clinical Manifestation

8. DISTRIBUTION OF MODE OF ONSET

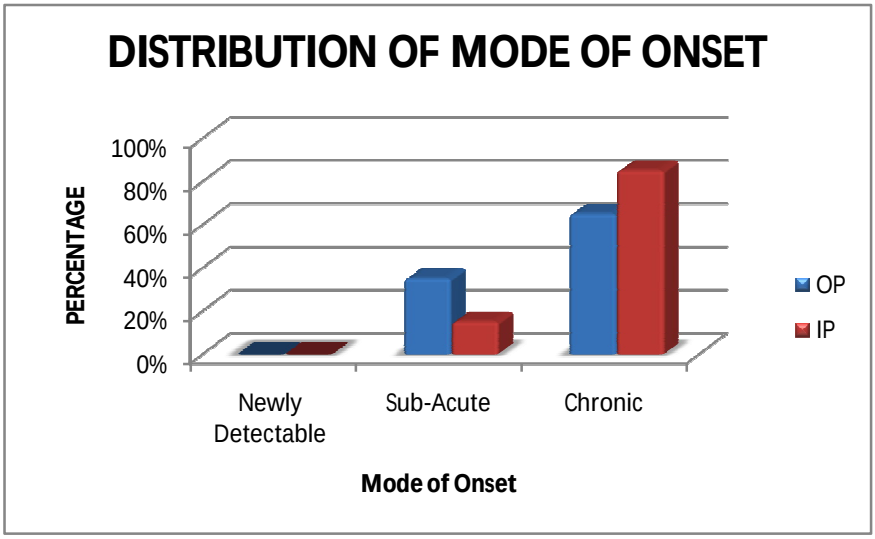
Table-8 illustrates the distribution of religion and its percentage.

TABLE-8

DISTRIBUTION OF MODE OF ONSET

Sl. No.	Mode of Onset	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Newly Detectable	-	-	-	-
2.	Sub-Acute	7	35%	3	15%
3.	Chronic	13	65%	17	85%
Total		**20**	**100%**	**20**	**100%**

FIGURE-8



The onset of Iya Neerizhivu ensues a chronic mode of onset with a relative percentage of 65%in OP and 85% in IP patients.

9. DISTRIBUTION OF DURATION OF ILLNESS

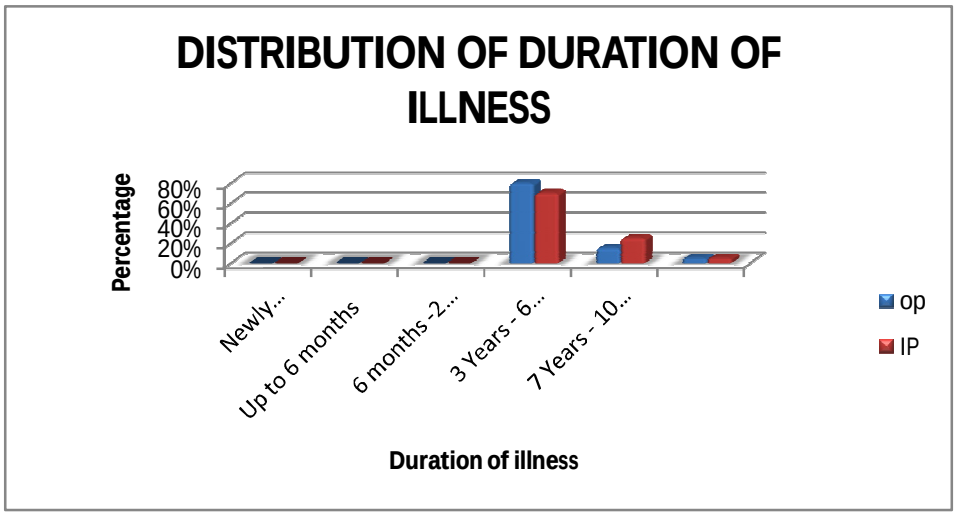
Table-9 illustrates the duration of illness and its percentage.

TABLE-9

DISTRIBUTION OF DURATION OF ILLNESS

Sl. No.	Duration of illness	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Newly Detectable	-	-	-	-
2.	Up to 6 months	-	-	-	-
3.	6 months -2 Years	-	-	-	-
4.	3 Years - 6 Years	16	80%	14	70%
5.	7 Years - 10 Years	3	15%	5	25%
6.	11 Years - 15 Years	1	5%	1	5%
	Total	**20**	**100%**	**20**	**100%**

FIGURE-9



Iya Neerizhivu greatly noticed in the 40 patients suffering with Iya Neerizhivu for about more than 3 years to 6 years. The percentage of 80% in OP and 70% in IP.

10. DISTRIBUTION OF FAMILY HISTORY

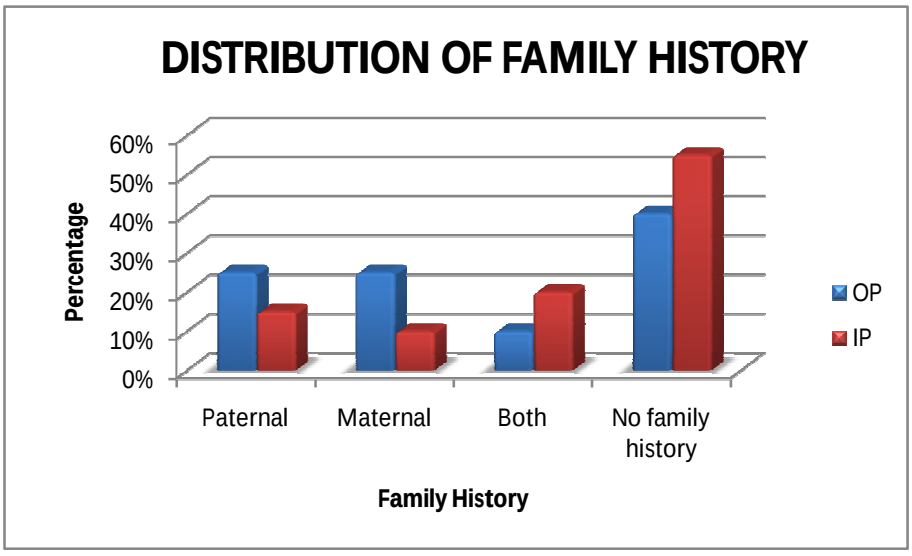
Table-10 illustrates the family history and its percentage.

TABLE-10

DISTRIBUTION OF FAMILY HISTORY

Sl. No.	Family History	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Paternal	5	25%	3	15%
2.	Maternal	5	25%	2	10%
3.	Both	2	10%	4	20%
4.	No family history	8	40%	11	55%
Total		**20**	**100%**	**20**	**100%**

FIGURE-10



The table links a family history with the incidence of Iya Neerizhivu with relative percentage among OP 30% had paternal history, 20% had maternal history, 15% had both and 35% had no family history. Among IP 20% had paternal history, 15% had maternal history, 5% had both and 60% had no family history.

11. **DISTRIBUTION OF HISTORY OF PREVIOUS TREATMENT OF NEERIZHIVU**

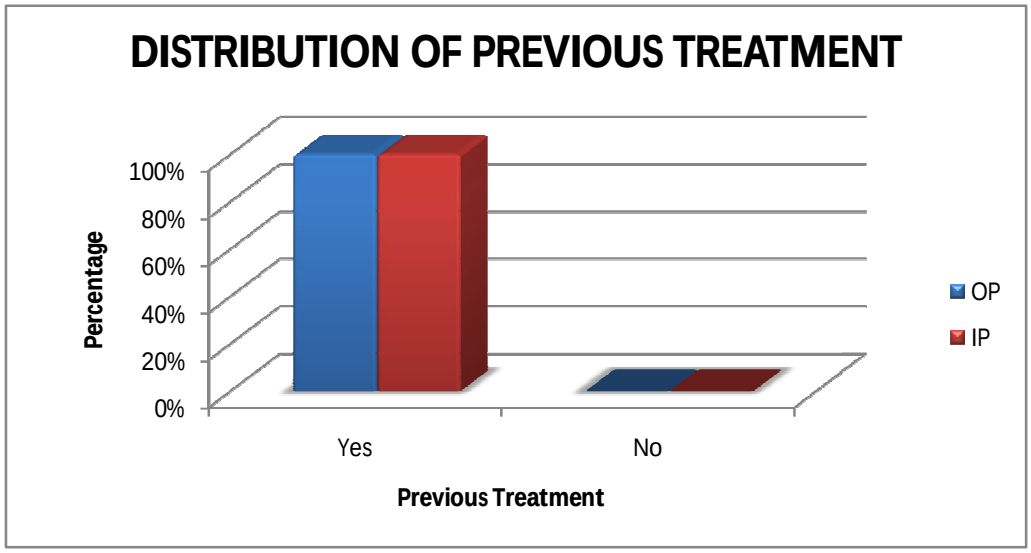
Table-11illustrates the previous treatment of Neerizhivu and its percentage.

TABLE-11

DISTRIBUTION OF PREVIOUS TREATMENT

Sl. No.	Previous Treatment	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Yes	20	100%	20	100%
2.	No	-	-	-	-
	Total	**20**	**100%**	**20**	**100%**

FIGURE-11



The table shows that 100% of OP and 100% of IP patients had a history of previous treatment for Neerizhivu.

12. DISTRIBUTION OF PERSONAL HISTORY

Table-12 illustrates the personal history and its percentage.

TABLE-12

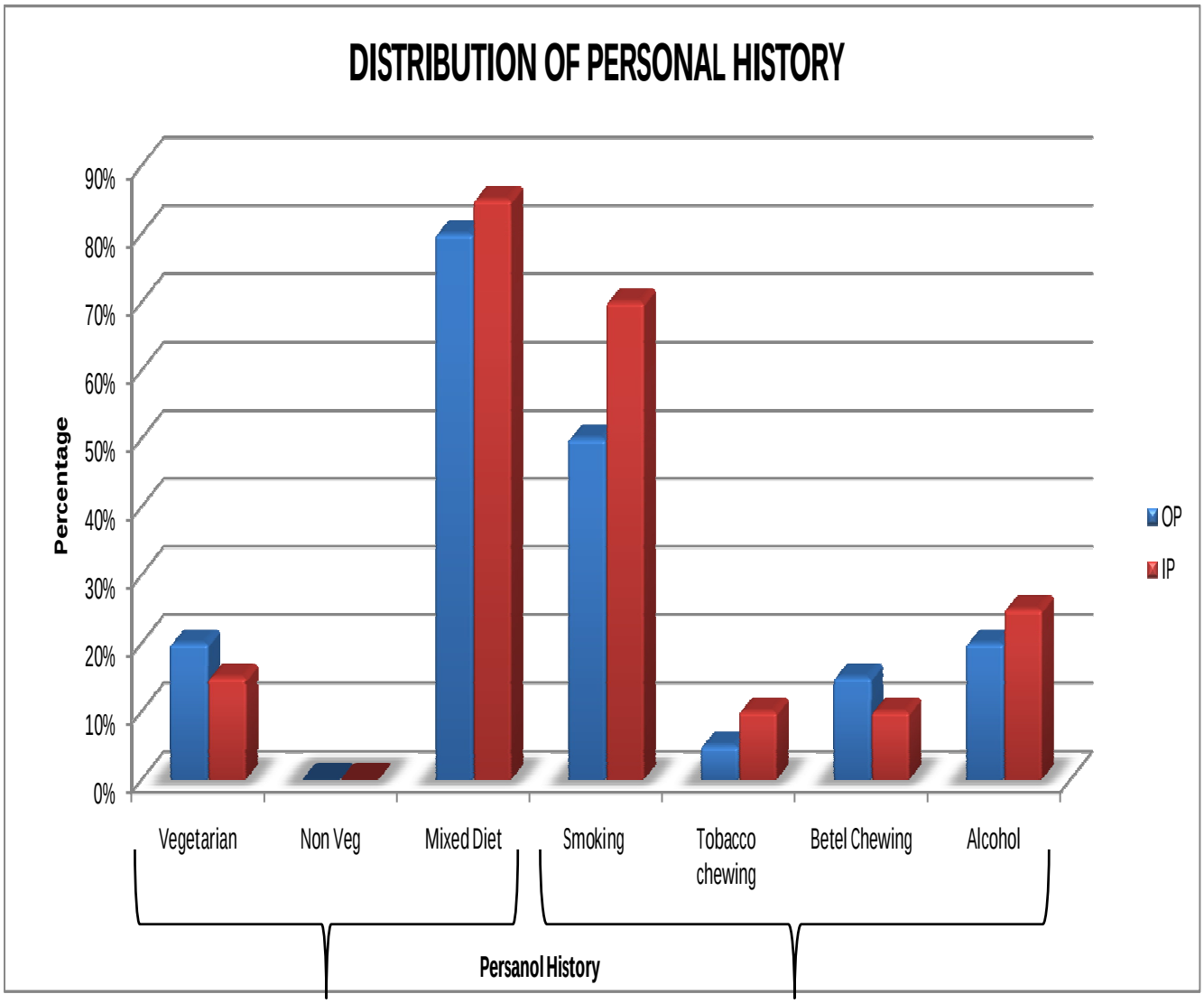
DISTRIBUTION OF PERSONAL HISTORY

Sl. No.	Personal History	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
DIET					
1.	Vegetarian	4	20%	3	15%
	Non Veg	-	-	-	-
	Mixed Diet	16	80%	17	85%
PERSONAL HABITS					
2.	Smoking	10	50%	14	70%
	Tobacco chewing	1	5%	2	10%
	Betel Chewing	3	15%	2	10%
	Alcohol	4	20%	5	25%

IyaNeerizhivu is reported greatly among 80% of OP and 85% of IP patients with habit of mixed diet.

In Personal Habits 50% of OP and 70%of IP patients had smoking habit, 10% of IP patients had tobacco chewing, 15% of OP and 10% of IP patients had betel chewing and 20% of OP and 25% of IP patients had alcohol consumption.

FIGURE-12


DISTRIBUTION OF PERSONAL HISTORY
Percentage
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
OP
IP
Vegetarian
Non Veg
Mixed Diet
Smoking
Tobacco chewing
Betel Chewing
Alcohol
Persanol History
DIET
PERSONAL HABITS

13. DISTRIBUTION OF SOCIO-ECONOMICAL STATUS

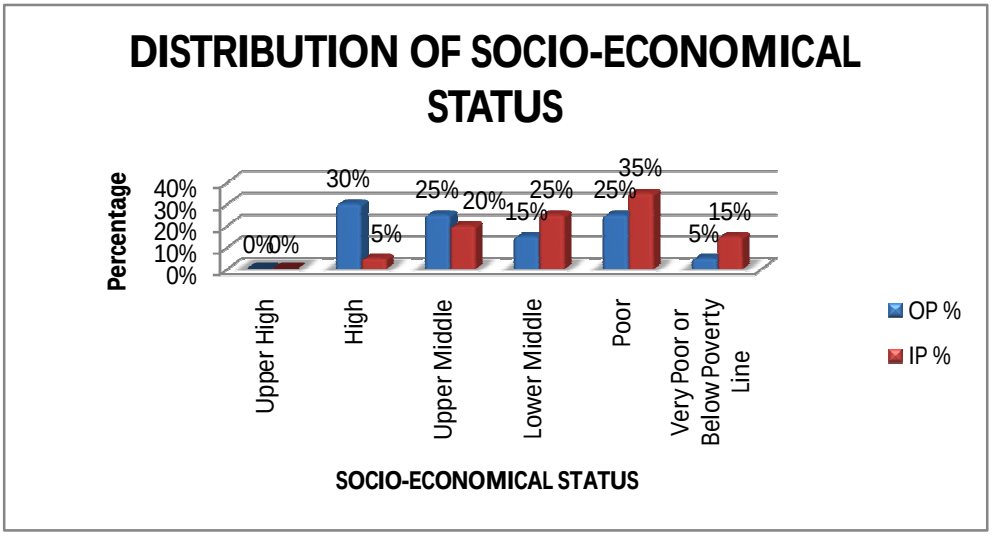
Table-13 illustrates the distribution of socio-economic status and its percentage.

TABLE-13

DISTRIBUTION OF SOCIO-ECONOMICAL STATUS

Sl. No.	Socio-Economical Status	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Upper High	-	-	-	-
2.	High	6	30%	1	5%
3.	Upper Middle	5	25%	4	20%
4.	Lower Middle	3	15%	5	25%
5.	Poor	5	25%	7	35%
6.	Very Poor or Below Poverty Line	1	5%	3	15%
Total		**20**	**100%**	**20**	**100%**

FIGURE-13



Among the 40 patients of the study group there is a marked percentage of the disease of the population of lower middle socio economic status in relative percentages of 15% were in OP and 25% were in IP.

14. DISTRIBUTION OF OTHER SYSTEM INVOLVEMENT

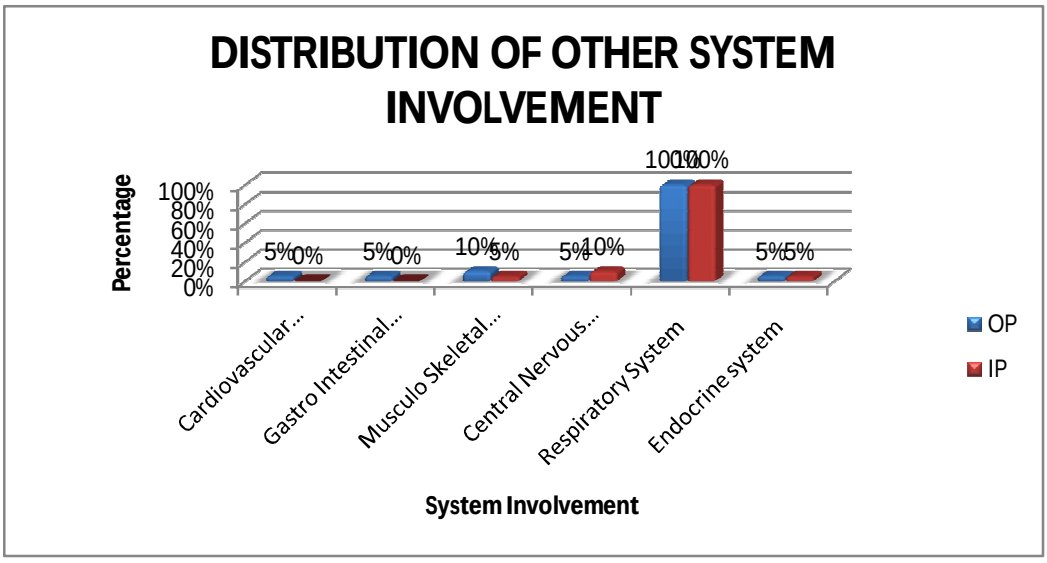
Table-14 illustrates the duration of illness and its percentage.

TABLE-14

DISTRIBUTION OF OTHER SYSTEM INVOLVEMENT

Sl. No.	System Involvement	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Cardiovascular System	1	5%	-	-
2.	Gastro Intestinal System	1	5%	-	-
3.	Musculo Skeletal System	2	10%	1	5%
4.	Central Nervous System	1	5%	2	10%
5.	Respiratory System	20	100%	20	100%
6.	Endocrine system	1	5%	1	5%

FIGURE-14



The table shows that the symptoms involving Respiratory System are greatly associated along with complaints of IyaNeerizhivu.

15. DISTRIBUTION OF BODY MASS INDEX

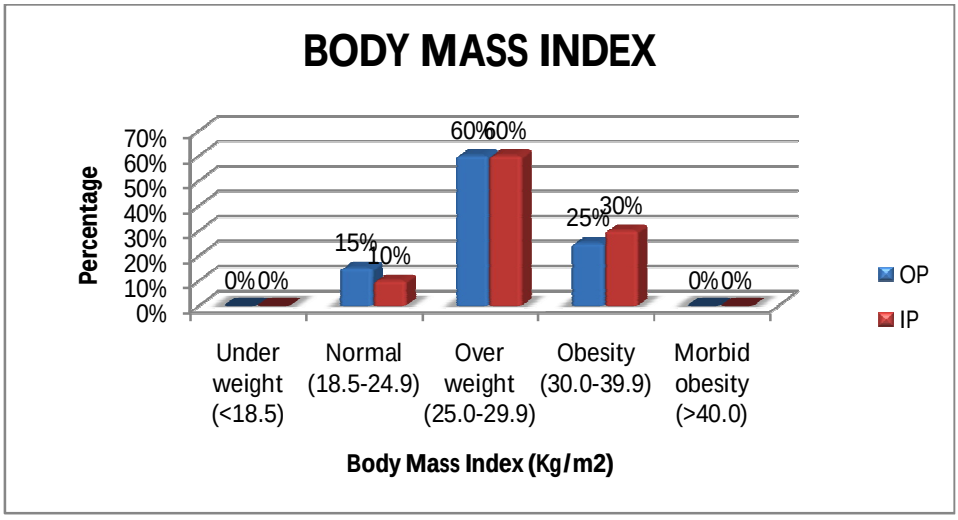
Table-15 illustrates the BMI and its relative percentage.

TABLE-15

BODY MASS INDEX

Sl. No.	Body Mass Index (Kg/m^2)	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Under weight (<18.5)	-	-	-	-
2.	Normal (18.5-24.9)	3	15%	2	10%
3.	Over weight (25.0-29.9)	12	60%	12	60%
4.	Obesity (30.0-39.9)	5	25%	6	30%
5.	Morbid obesity (>40.0)	-	-	-	-
Total		**20**	**100%**	**20**	**100%**

FIGURE-15



The table shows that the body mass index among the 40 patients of the study group patients had normal BMI 15% in OP and 10% in IP. 60% in OP and 60% in IP patients had over weight (Class-I &II). 25% in OP and 30% in IP patients showed obesity in Iya Neerizhivu.

16. DISTRIBUTION OF CONSTITUTION OF BODY

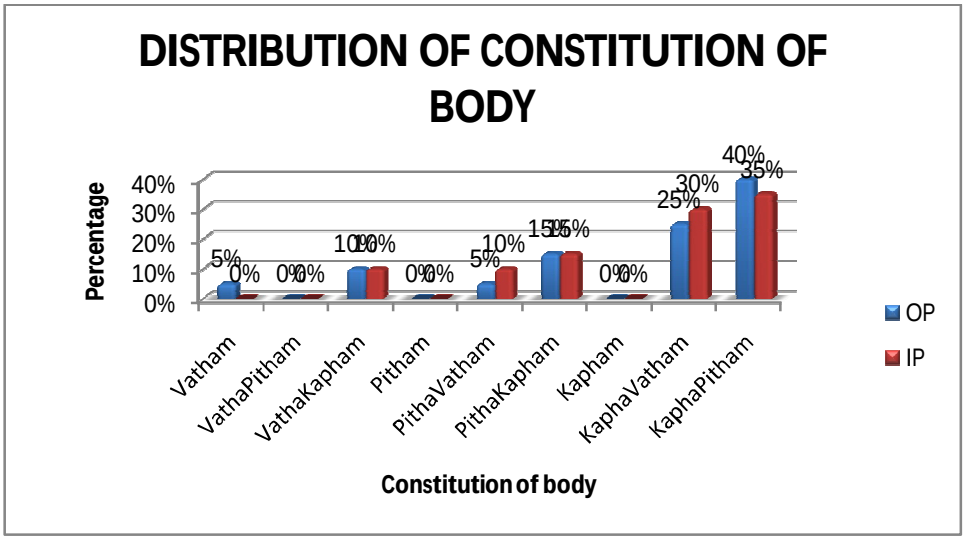
Table-16 illustrates the constitution of the body and its percentage.

TABLE-16

DISTRIBUTION OF CONSTITUTION OF BODY

Sl. No.	Constitution of body	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Vatham	1	5%	-	-
2.	Vatha Pitham	-	-	-	-
3.	Vatha Kapham	2	10%	2	10%
4.	Pitham	-	-	-	-
5.	Pitha Vatham	1	5%	2	10%
6.	Pitha Kapham	3	15%	3	15%
7.	Kapham	-	-	-	-
8.	KaphaVatham	5	25%	6	30%
9.	Kapha Pitham	8	40%	7	35%
	Total	**20**	**100%**	**20**	**100%**

FIGURE-16



From the above table, it is observed that highest incidence of Iya Neerizhivu among 20 Out patients were Vatha PithaThegi with 25%, Pitha VathaThegi with 30%, Kapha Pitham with 25 % and Kapha Vatham 10%. Among 20% In patients Pitha Vatha Thegi with 50%, Vatha Pitha Thegi with 30%, Kapha Pitham with 15 % and Kapha Vatham 10%.

17. DISTRIBUTION OF GUNAM

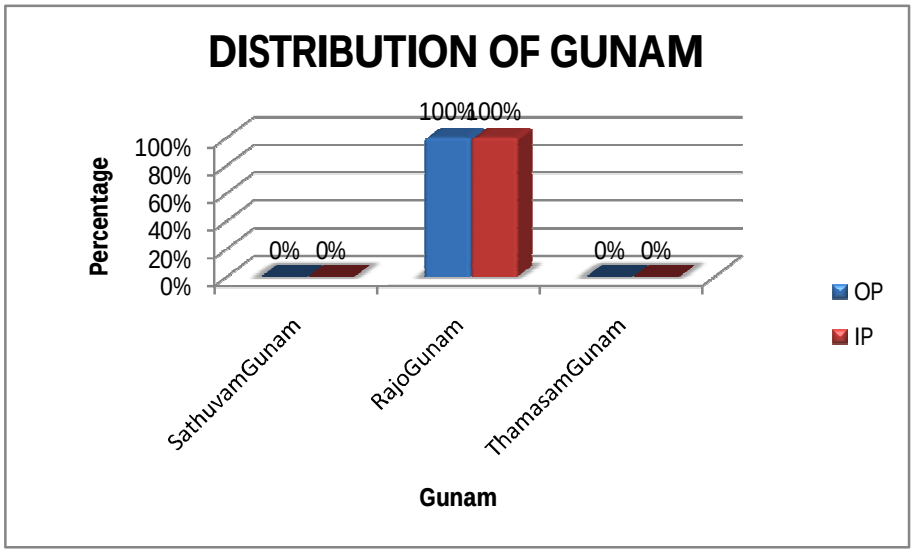
Table-17 illustrates the gunam and its percentage.

TABLE-17

DISTRIBUTION OF GUNAM

Sl. No.	Gunam	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Sathuvam Gunam	-	-	-	-
2.	Rajo Gunam	20	100%	20	100%
3.	Thamasam Gunam	-	-	-	-
Total		**20**	**100%**	**20**	**100%**

FIGURE-17



From the above table, it is observed that highest incidence of Iya Neerizhivu among Out patients and In patients with cent percent belongs to Rajo Gunam.

18. DISTRIBUTION OF KAALAM

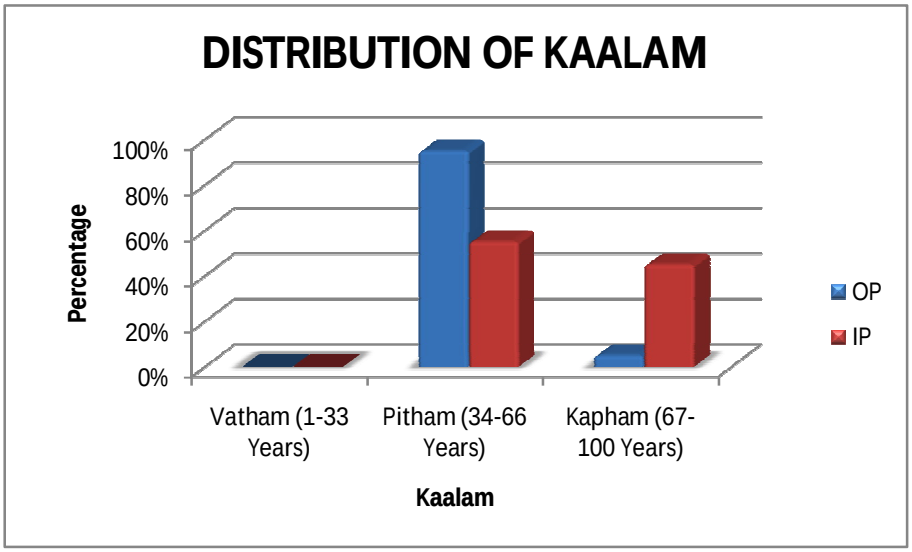
Table-18 illustrates the distribution of kaalam and its percentage.

TABLE-18

DISTRIBUTION OF KAALAM

Sl. No.	Kaalam	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Vatham (1-33 Years)	-	-	-	-
2.	Pitham (34-66 Years)	19	95%	11	55%
3.	Kapham (67- 100 Years)	1	5%	9	45%
Total		**20**	**100%**	**20**	**100%**

FIGURE-18



From the above table, it is observed that the highest incidence of IyaNeerizhivu among 20 Out patients is in Pitha Kaalam with 95%, Kapha Kaalam with 5%. Among 20In patients, is also Pitha Kaalam with 55%, Kapha Kaalam with 45%.

19. **DISTRIBUTION OF PARUVA KAALAM**

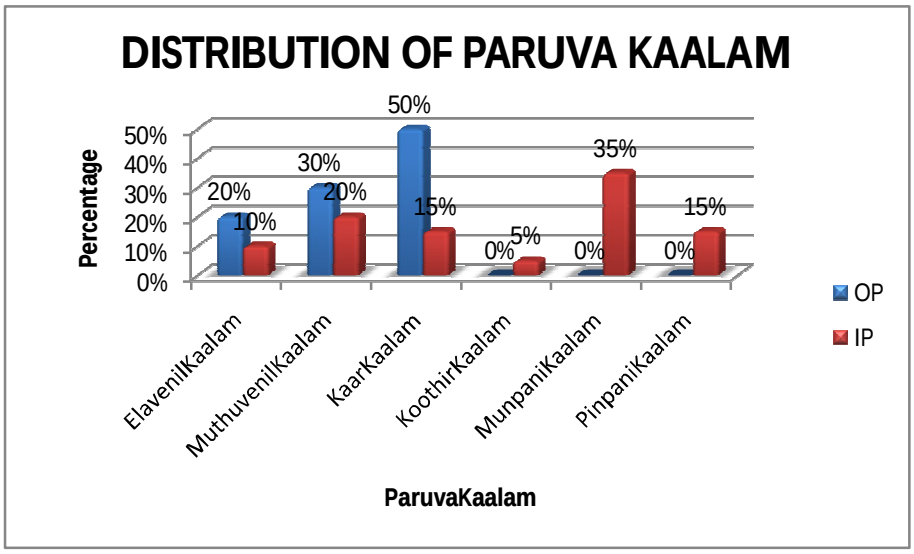
Table-19 illustrates the paruva kaalam and its percentage.

TABLE-19

DISTRIBUTION OF PARUVA KAALAM

Sl. No.	ParuvaKaalam	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Elavenil Kaalam	4	20%	2	10%
2.	Muthuvenil Kaalam	6	30%	4	20%
3.	Kaar Kaalam	10	50%	3	15%
4.	Koothir Kaalam	-	-	1	5%
5.	Munpani Kaalam	-	-	7	35%
6.	Pinpani Kaalam	-	-	3	15%
	Total	**20**	**100%**	**20**	**100%**

FIGURE-19



From the above table, it is observed that highest incidence of Iya Neerizhivu among 20 Out patients high incidence of the disease is in Kaar Kaalam50% and among 20 In patient were in Munpani Kaalam 35%.

20. DISTRIBUTION OF THINAI

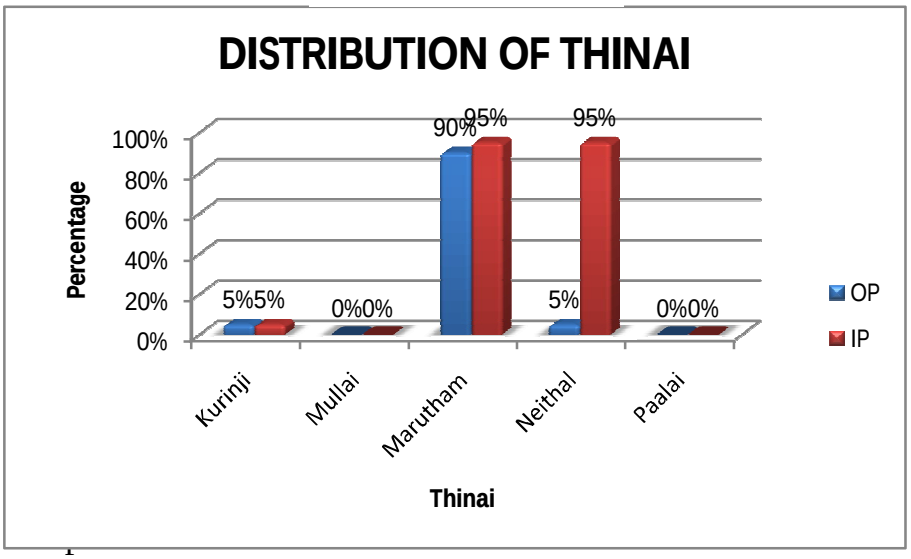
Table-20 illustrates the thinai and its percentage.

TABLE-20

DISTRIBUTION OF THINAI

Sl. No.	Thinai	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Kurinji	1	5%	1	5%
2.	Mullai	-	-	-	-
3.	Marutham	18	90%	19	95%
4.	Neithal	1	5%	-	-
5.	Paalai	-	-	-	-
	Total	**20**	**100%**	**20**	**100%**

FIGURE-20



From the above table, it is observed that highest incidence of Iya Neerizhivu among 20 Out patients were in the Marutham land with 90% and among In Patients also in Marutham land with 95%.

21. DISTRIBUTION OF MUKKUTRAM

(a). DERANGEMENT OF VATHAM

Table-21(a) illustrates the Derangement of Vatham and its percentage.

TABLE-21 (a)

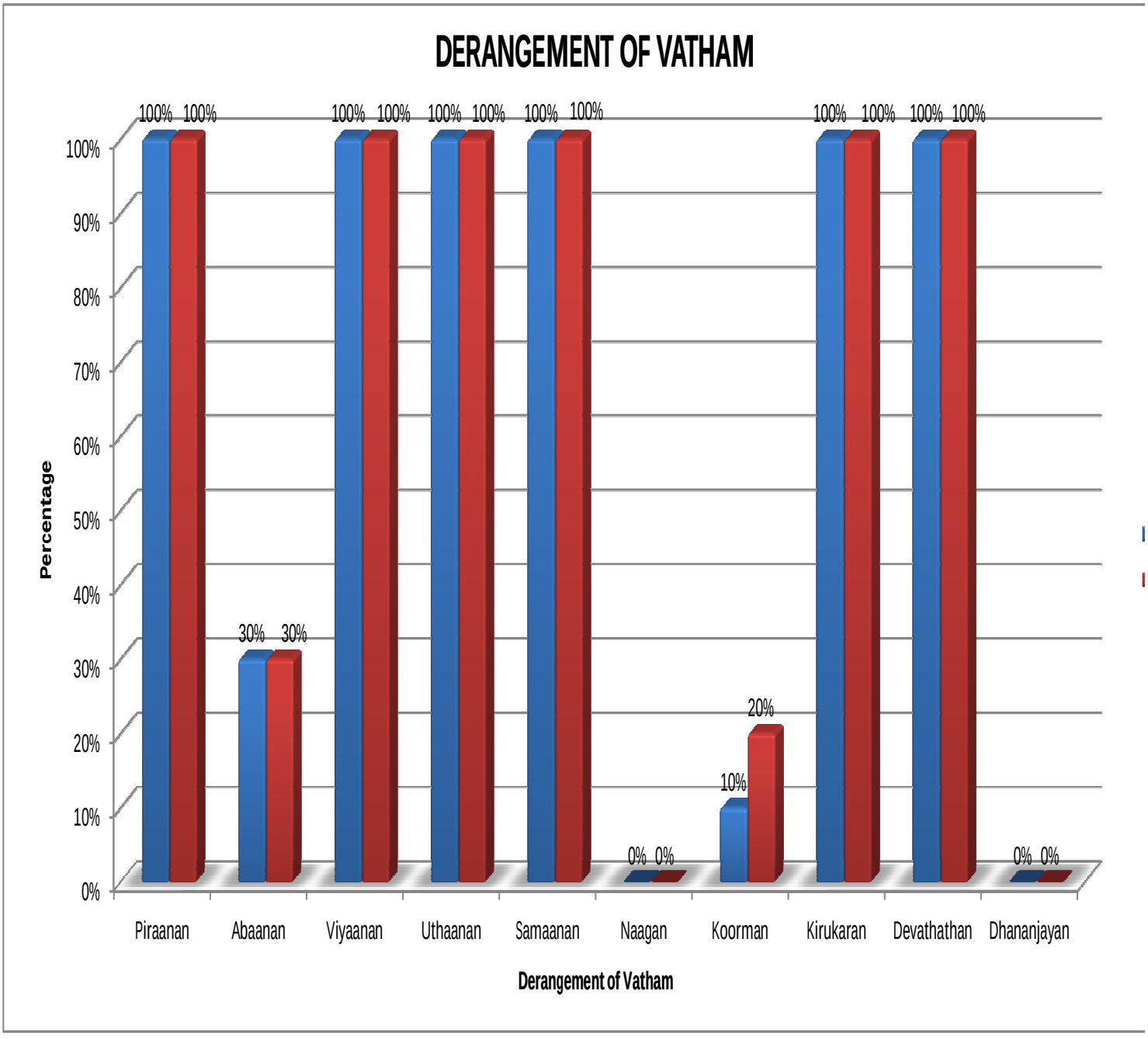
DERANGEMENT OF VATHAM

Sl. No.	Derangement of Vatham	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Piraanan	20	100%	20	100%
2.	Abaanan	6	30%	6	30%
3.	Viyaanan	20	100%	20	100%
4.	Uthaanan	20	100%	20	100%
5.	Samaanan	20	100%	20	100%
6.	Naagan	-	-	-	-
7.	Koorman	2	10%	4	20%
8.	Kirukaran	20	100%	20	100%
9.	Devathathan	20	100%	20	100%
10.	Dhananjayan	-	-	-	-

From the above table, it is observed that among 20 out patients 100% were affected in Piraanan, Viyaanan, Uthaanan, Samaanan, Kirukaran and Devathathan. Among 20 in patients 100% were affected in Piraanan, Viyaanan, Uthaanan, Samaanan, Kirukaran and Devathathan.

FIGURE-21 (a)

CONDITION OF VATHAM



21 (b) DERANGEMENT OF PITHAM

Table-21 (b) illustrates thederangement of pitham and its percentage.

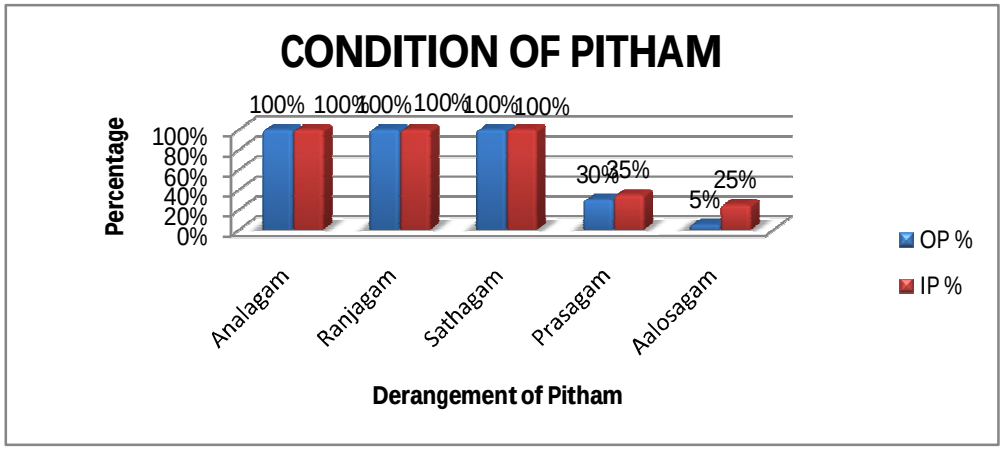
TABLE-21 (b)

DERANGEMENT OF PITHAM

Sl. No.	Derangement of Pitham	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Analagam	20	100%	20	100%
2.	Ranjagam	20	100%	20	100%
3.	Sathagam	20	100%	20	100%
4.	Prasagam	6	30%	7	35%
5.	Aalosagam	1	5%	5	25%

FIGURE-21 (b)

CONDITION OF PITHAM



From the above table, it is observed that among 20 out patients 100% were affected in Analagam, Ranjagam and Sathagam; 30% were affected in Prasagam; 5% were affected in Aalosagam Among 20 In patients 100% were affected in Analagam, Ranjagam and Sathagam 35% were affected in Prasagam 25% were affected in Aalosagam.

21 (c) DERANGEMENT OF KAPHAM

Table-21 (c) illustrates the kapham and its percentage.

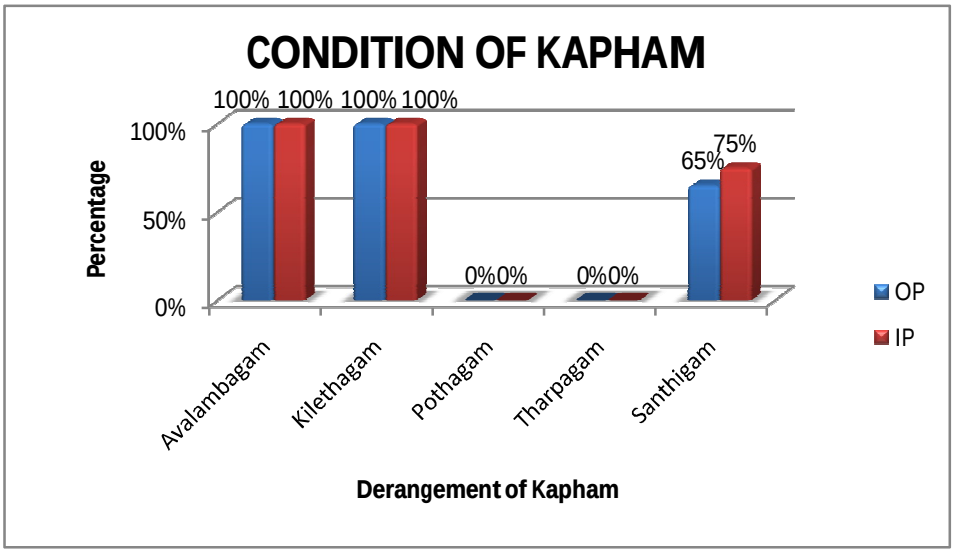
TABLE-21 (c)

DERANGEMENT OF KAPHAM

Sl. No.	Derangement of Kapham	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Avalambagam	20	100%	20	100%
2.	Kilethagam	20	100%	20	100%
3.	Pothagam	-	-	-	-
4.	Tharpagam	-	-	-	-
5.	Santhigam	13	65%	15	75%

FIGURE-21 (c)

CONDITION OF KAPHAM



From the above table, it is observed that among 20 out patients 100% were affected in Avalambagam and Kilethagam; 65% were affected in Santhigam. Among 20 in patients100% were affected in Avalambagam and Kilethagam 75% were affected in Santhigam.

22. DISTRIBUTION OF INVOLVEMENT OF UDAL THATHUKKAL

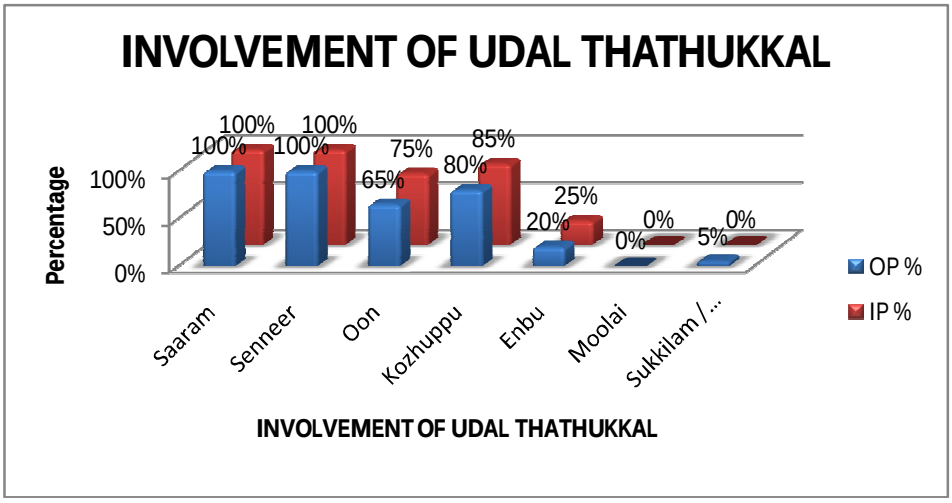
Table-22 illustrates the involvement of udalthathukkal and its percentage.

TABLE-22

INVOLVEMENT OF UDAL THATHUKKAL

Sl. No.	Involvement of UdalThathukkal	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Saaram	20	100%	20	100%
2.	Senneer	20	100%	20	100%
3.	Oon	13	65%	15	75%
4.	Kozhuppu	16	80%	17	85%
5.	Enbu	13	75%	15	75%
6.	Moolai	-	-	-	-
7.	Sukkilam / Suronitham	1	5%	-	-

FIGURE-22



From the above table, it is observed that among 20 out patients 100% were affected in Saaram and Senneer, 80% were affected in Kozhuppu and 65% were affected in Enbu. Among 20 in patients 100% were affected in Saaram and Senneer, 85% were affected in Kozhuppu and 75% were affected in Enbu.

23. DISTRIBUTION OF KANMENTHIRIYAM

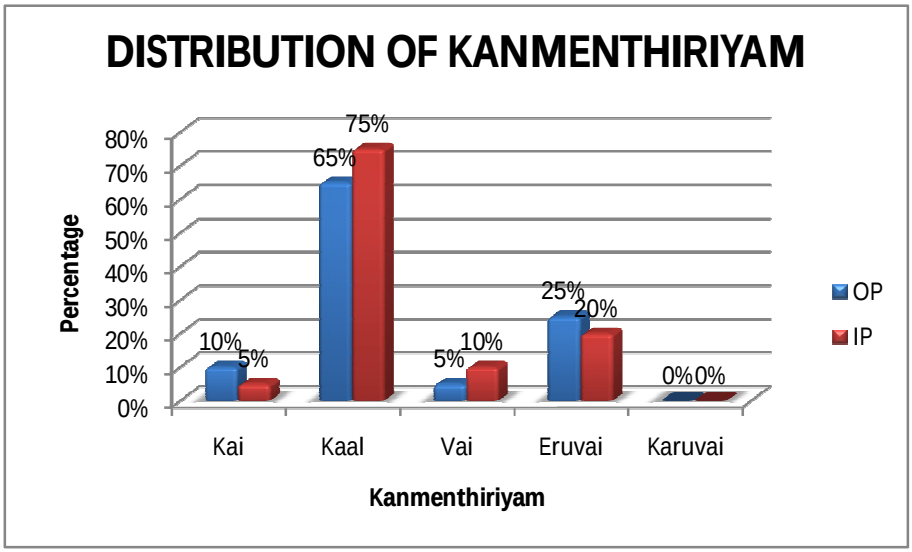
Table-23 illustrates the kanmenthiriyam and its percentage.

TABLE-23

DISTRIBUTION OF KANMENTHIRIYAM

Sl. No.	Kanmenthiriyam	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Kai	2	10%	1	5%
2.	Kaal	13	65%	15	75%
3.	Vai	1	5%	2	10%
4.	Eruvai	5	25%	4	20%
5.	Karuvai	-	-	-	-

FIGURE-23



From the above table, it is observed that among 20 Out patients, 65% were affected in Kaal and 25% inEruvai. Among 20 in patients 75% were affected in Kaal and 20% in Eruvai.

24. DISTRIBUTION OF IMPORIGAL(GNANENDRIUM)

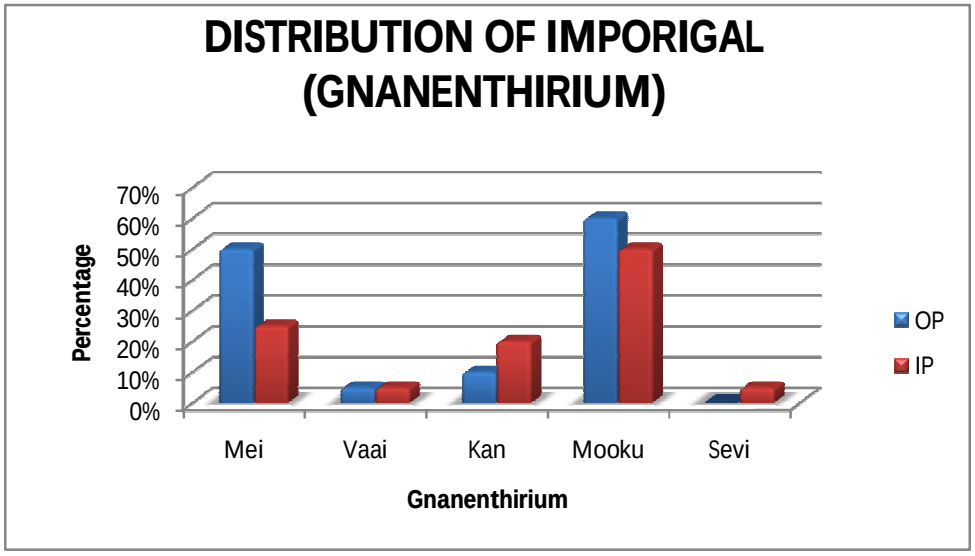
Table-24 illustrates the gnanenthirium and its percentage.

TABLE-24

DISTRIBUTION OF IMPORIGAL (GNANENTHIRIUM)

Sl. No.	Gnanenthirium	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Mei	10	50%	5	25%
2.	Vaai	1	5%	1	5%
3.	Kan	2	10%	4	20%
4.	Mooku	12	60%	10	50%
5.	Sevi	-	-	1	5%

FIGURE-24



From the above table, it is observed that among 20 out patients and 20 in patients 50% and 25% were affected in Mei. Among 20 out patients 10% and 20 in patients 20% were affected in Kan.

25. DISTRIBUTION OF KOSAM

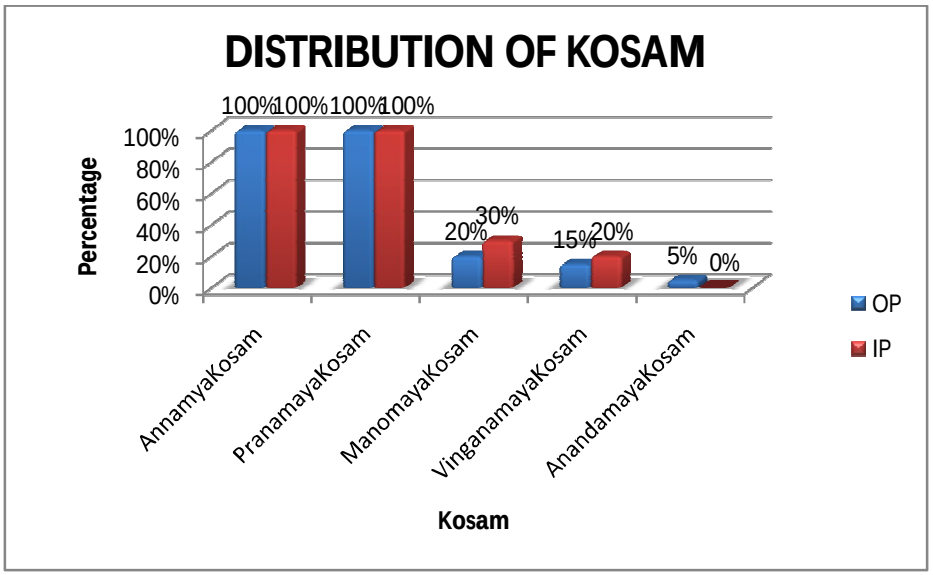
Table-25 illustrates the kosam and its percentage.

TABLE-25

DISTRIBUTION OF KOSAM

Sl. No.	Kosam	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Annamya Kosam	20	100%	20	100%
2.	Pranamaya Kosam	20	100%	20	100%
3.	Manomaya Kosam	4	20%	6	30%
4.	Vinganamaya Kosam	3	15%	4	20%
5.	Anandamaya Kosam	1	5%	-	-

FIGURE-25



From the above table, it is observed that among 20 Out patients 100% were affected in Annamaya Kosam, 40% were affected in Manomaya Kosam and 30% affected in Vinganamaya kosam. Among 20 in patients, 100% were affected in Annamaya Kosam, 35% were affected in Manomaya Kosam and 30% were affected in Vinganamaya Kosam

26. DISTRIBUTION OF CONDITIONS OF ENVAGAI THERVUGAL

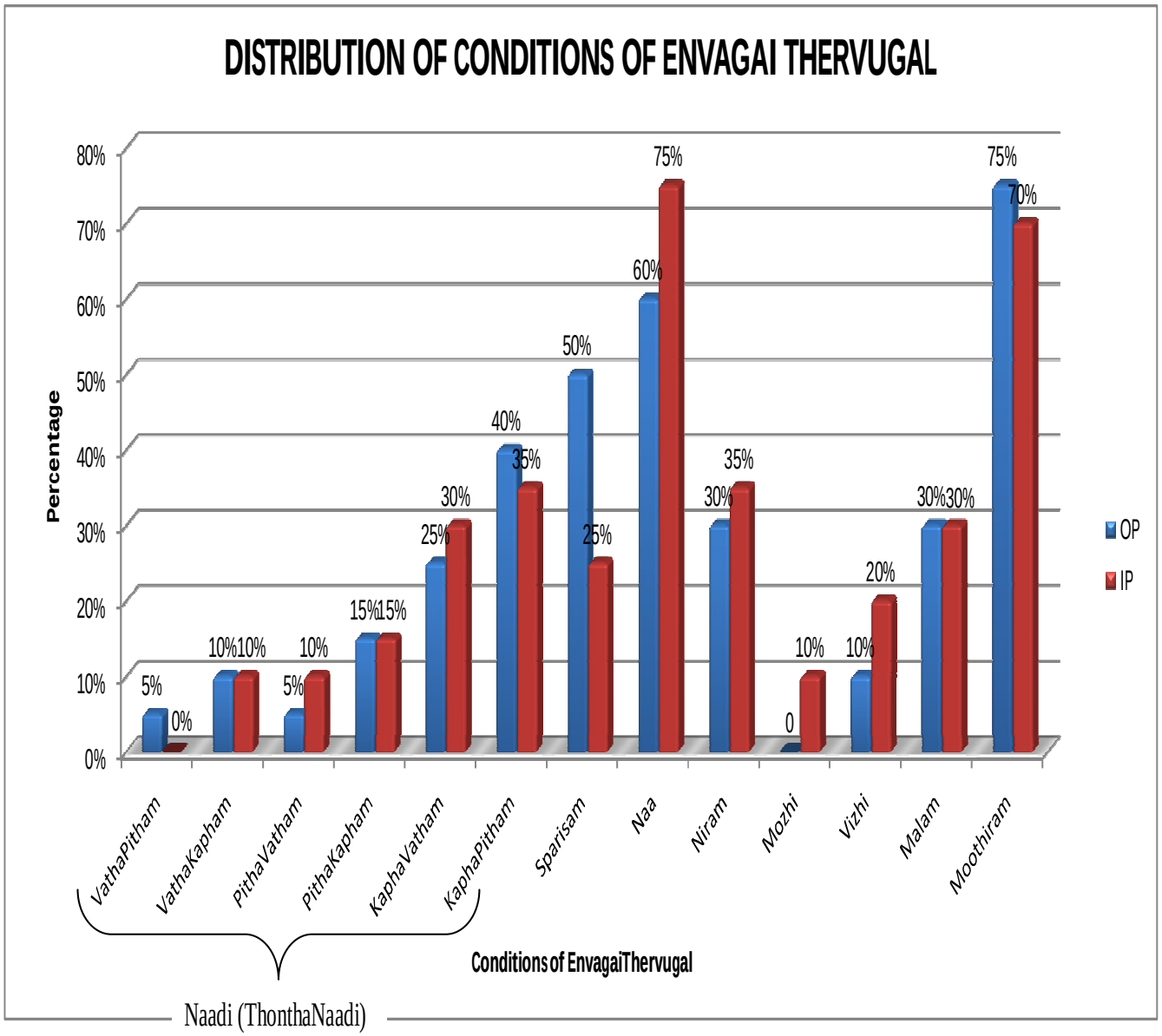
Table-26 illustrates the envagaithervugal and its percentage.

TABLE-26

DISTRIBUTION OF CONDITIONS OF ENVAGAI THERVUGAL

Sl. No.	Conditions of EnvagaiThervugal	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Naadi (Thontha Naadi)				
	1). Vatha Pitham	1	5%	-	-
	2). Vatha Kapham	2	10%	2	10%
	3). Pitha Vatham	1	5%	2	10%
	4). Pitha Kapham	3	15%	3	15%
	5). Kapha Vatham	5	25%	6	30%
	6). Kapha Pitham	8	40%	7	35%
2.	Sparisam	10	50%	5	25%
3.	Naa	12	60%	15	75%
4.	Niram	6	30%	7	35%
5.	Mozhi	-	-	2	10%
6.	Vizhi	2	10%	4	20%
7.	Malam	6	30%	6	30%
8.	Moothiram	15	75%	14	70%

From the above table it is observed that among 20 out patients 40% had Kapha Pitha Naadi, 25% had Kapha Vatha Naadi, 10% had Vatha Kapha Naadi and 15% had Pitha Kapha Vatha Naadi; 100% were affected in Naa and Moothiram; 50% were affected in Sparisam; 30% were affected in Niram and Malam; 10% were affected in Vizhi. Among 20 In patients 50% had Pitha Vatha Naadi, 20% had Vatha Pitha Naadi and 30% had Kapha Vatha Naadi; 100% were affected in Naa and Moothiram; 25% were affected in Sparisam; 35% were affected in Niram; 30% were affected in Malam; 20% were affected in Vizhi.


DISTRIBUTION OF CONDITIONS OF ENVAGAI THERVUGAL
Percentage
80%
70%
60%
50%
40%
30%
20%
10%
0%
5%
0%
10%
10%
5%
10%
15%
15%
25%
30%
40%
35%
50%
25%
60%
75%
30%
35%
0
10%
10%
20%
30%
30%
75%
70%
OP
IP
VathaPitham
VathaKapham
PithaVatham
PithaKapham
KaphaVatham
KaphaPitham
Sparisam
Naa
Niram
Mozhi
Vizhi
Malam
Moothiram
Conditions of EnvagaiThervugal
Naadi (ThonthaNaadi)

27. DISTRIBUTION OF NEER KURI

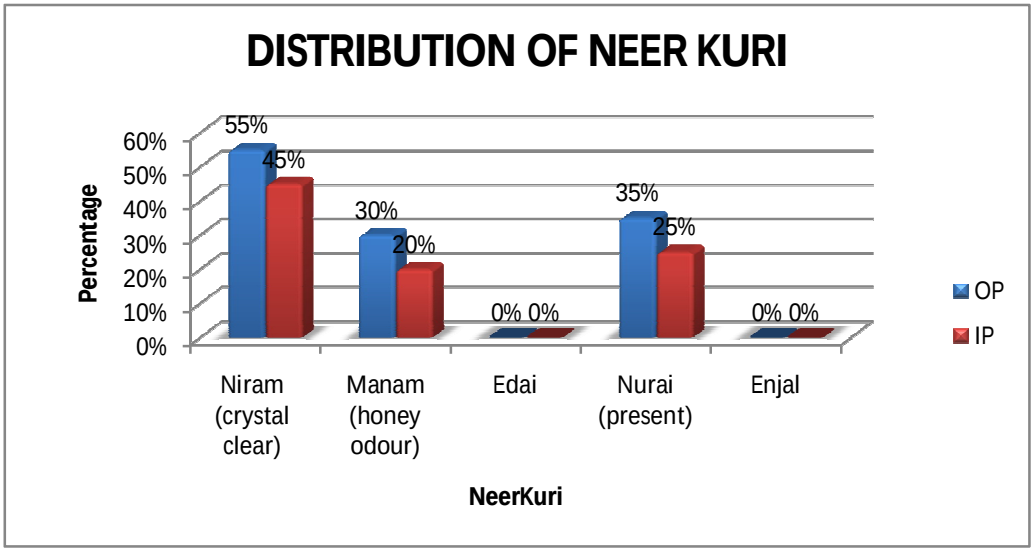
Table-27 illustrates the neerkuri and its percentage.

TABLE-27

DISTRIBUTION OF NEER KURI

Sl. No.	NeerKuri	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Niram (crystal clear)	11	55%	9	45%
2.	Manam (honey odour)	6	30%	4	20%
3.	Edai	-	-	-	-
4.	Nurai (present)	7	35%	5	25%
5.	Enjal	-	-	-	-

FIGURE-27



From the above table, it is observed in Neerkuri that, among 20 Out patients 55% were affected in Niram; 30% were affected in manam; 35% were affected in Nurai.Among 20 In patients 45% were affected in Niram; 20% were affected in Manam and Nurai.

28. DISTRIBUTION OF NEI KURI

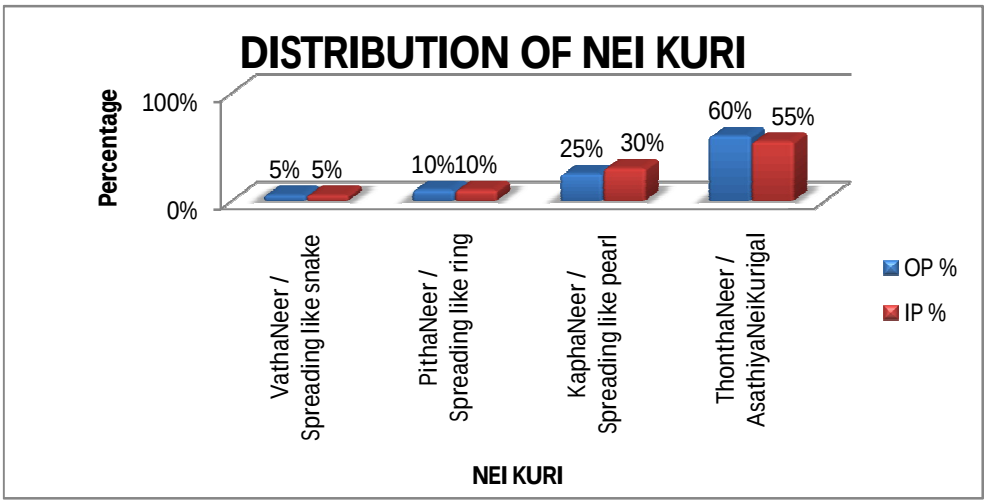
Table-28 illustrates the neikuri and its percentage.

TABLE-28

DISTRIBUTION OF NEI KURI

Sl. No.	NeiKuri	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Vatha Neer / Spreading like snake	2	10%	3	15%
2.	Pitha Neer / Spreading like ring	7	35%	6	30%
3.	Kapha Neer / Spreading like pearl	8	40%	9	45%
4.	Thontha Neer / AsathiyaNeiKurigal	3	15%	2	10%
Total		**20**	**100%**	**20**	**100%**

FIGURE-28



Among 20 OP patients showed 15% of Thontha Neer; 40% of Kapha Neer; 35% of Pitha Neer; 10% of Vatha Neer. Among 20 IP patients showed 10% of Thontha Neer; 45% of Kapha Neer; 30% of Pitha Neer; 15% of Vatha Neer features in Neikuri observation in Iya Neerizhivu.

SOME SHAPES FOUND ON NEIKURI EXAMINATION OF IYA NEERIZHIVU AMONG OP & IP PATIENTS

29. DISTRIBUTION OF LABORATORY ANALYSIS

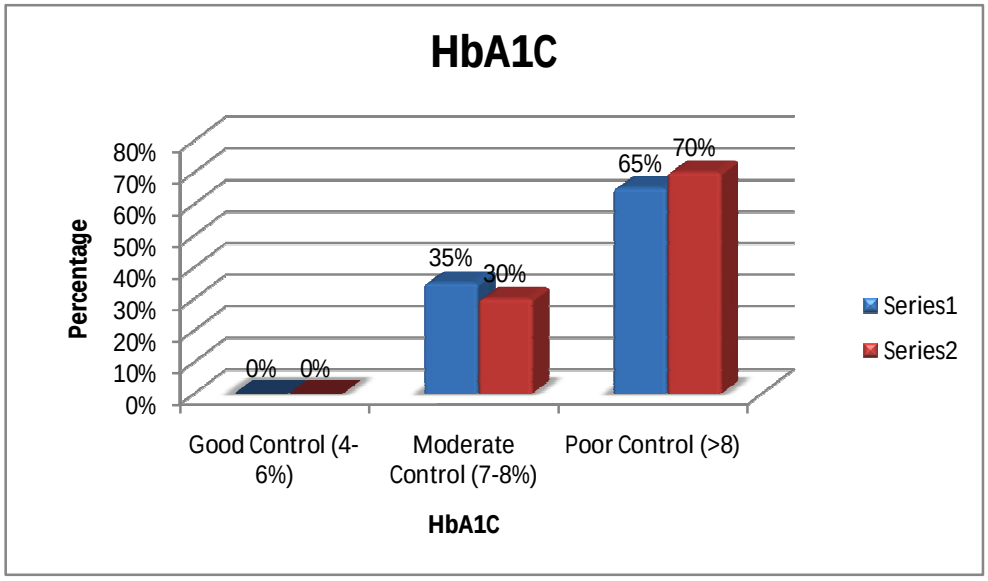
Table-29 (a) illustrates the reference of HbA1C and its percentage.

TABLE-29

HbA1C

Sl. No.	HbA1C	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Good Control (4-6%)	-	-	-	-
2.	Moderate Control (7-8%)	7	35%	6	30%
3.	Poor Control (>8)	13	65%	14	70%
Total		**20**	**100%**	**20**	**100%**

FIGURE-29



The table shows among 20 out patients 65% had poor control and 35% had fair control, among 20 In patients 70% had poor control and 30% had moderate control of HbA1C in recruitment of study.

30. DISTRIBUTION OF SUB TYPES OF NEERIZHIVU

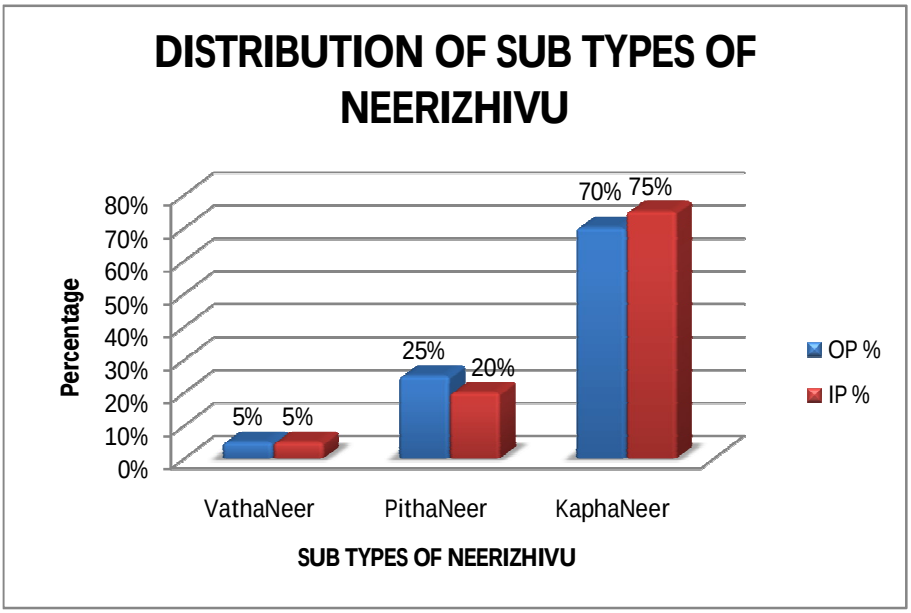
Table-30 illustrates the distribution of subtype of Neerizhivu and its percentage.

TABLE-30

DISTRIBUTION OF SUB TYPES OF NEERIZHIVU

Sl. No.	Sub Types of Madhumegam	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Vatha Neer	1	5%	1	5%
2.	Pitha Neer	5	25%	4	20%
3.	Kapha Neer	14	70%	15	75%
	Total	**20**	**100%**	**20**	**100%**

FIGURE-30



The table shows that high prevalence of the 40 patients recruited in the study different sub types of Neerizhivu diagnosed by signs and symptoms, Nadi& Urine, examination in cases of Iya Neerizhivu. 70% of OP and 75% of IP were Kapha type of Neerizhivu. 25% of OP and 20% of IP were Pitha type of Neerizhivu.

31. GRADATION OF RESPONSE

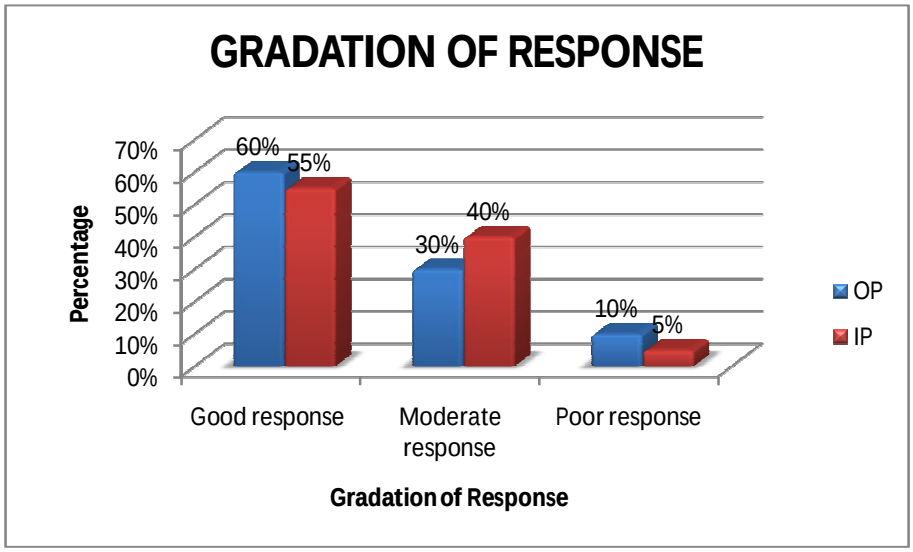
Table-32illustrates the Gradation of Results and its percentage

TABLE-31

GRADATION OF RESPONSE

Sl. No.	Gradation of Response	Out Patients (OP)		In Patients (IP)	
		No. of cases	Percentage (%)	No. of cases	Percentage (%)
1.	Good response	12	60%	11	55%
2.	Moderate response	6	30%	8	40%
3.	Poor response	2	10%	1	5%
	Total	**20**	**100%**	**20**	**100%**

FIGURE-31



Among the 40 patients included in the study 85% of Outpatients and 55% of in patients had good results. 15% of out patients and 40% of in patients had moderate response and 5% in patients showed poor response

OUT-PATIENT CASE SHEET: 20 PATIENTS TREATED IN OP FOR IYA NEERIZHIVU

Sl. No.	OP No.	Name	Age / Sex	Occupation	Duration of Illness	Date of Onset of Treatment	Date of Treminatio n of Treatment	Total Days	Results
1.	32101	Shangar	65/M	Cook	8 Years	06.04.2017	16.08.2017	95	Moderate
2.	37549	Muththu	63/M	Retd. Postmaster	5 Years	26.04.2017	21.08.2017	91	Good
3.	40810	Ramapandiyan	65/M	Land broker	4 Years	08.05,2017	30.08.2017	91	Good
4.	40847	Balasunthari	55/F	Nurse	5 Years	08.05.2017	14.09.2017	92	Good
5.	52651	Kanthavel	48/M	Driver	3 Years	19.06.2017	30.10.2017	98	Poor
6.	58024	Perumal	73/M	Retd. Police	10 Years	07.07.2017	17.11.2017	96	Moderate
7.	59223	Ganthimathy	61/F	Housewife	4 Years	11.07.2017	16.12.2017	90	Good
8.	59746	Suriyakala	48/F	Cook	3 Years	13.07.2017	02.12.2017	94	Moderate
9.	61703	Suppammal	61/F	Beedi maker	7 Years	19.07.2017	16.11.2017	99	Poor
10.	63884	Thagira	40/F	Housewife	3 Years	26.07.2017	16.11.2017	90	Good
11.	66783	Muththulaxmi	48/F	Housewife	2 Years	05.08.2017	02.12.2017	91	Good
12.	71009	Rajinidevi	56/F	Tailar	3 Years	19.08.2017	09.11.2017	92	Good
13.	71838	Pazanisamy	64/M	Cooley	5 Years	22.08.2017	06.12.2017	96	Moderate
14.	71949	Peshimuththu	60/M	Welding worker	6 Years	22.08.2018	06.12.2017	97	Moderate
15.	74507	Mani	61/F	Painter	7 Years	30.08.2017	19.12.2017	98	Moderate
16.	75203	Vasantha	55/F	Housewife	5 Years	01.09.2017	20.12.2017	90	Good
17.	76426	Seenivashan	51/M	Clark	3 Years	05.09.2017	28.12.2017	91	Good
18.	76581	Manommani	60/F	Cook	4 Years	06.09.2017	13.12.2017	92	Good
19.	82948	Chanthanakumar	52/M	Clark	4 Years	25.09.2017	16.12.2017	83	Good
20.	85387	Sangarammal	56/F	Housewife	3 Years	26.09.2017	18.12.2017	84	Good

IN-PATIENT CASE SHEET: 20 PATIENTS TREATED IN IP FOR IYA NEERIZHIVU

Sl. No.	IP No.	Name	Age / Sex	Occupation	Duration of Illness	Date of Admission	Date of Discharge	No. of Days		Total Days	Results
								IP	OP		
1.	1135	Rajam	60/F	Cooley	5 years	18/04/2017	02/06/2017	55	35	90	Good
2.	1737	Sangaran	70/M	Cooley	4 years	14/06/2017	04/07/2017	20	72	92	Moderate
3.	1779	Thangaraj	65/M	Cook	5 years	17/06/2017	21/07/2017	35	64	99	Poor
4.	1871	Pisshumani	59/M	Cooley	4 years	28/06/2017	17/07/2017	19	71	90	Good
5.	1957	Thaivakambar	71/M	Tailar	7 years	05/07/2017	14/07/2017	10	85	95	Moderate
6.	2234	Shangar	70/M	Milk man	6 years	09/08/2017	29/08/2017	20	72	92	Good
7.	2441	Thurairaj	65/M	Cook	7 years	30/08/2017	20/09/2017	21	70	91	Moderate
8.	2612	Akpar	70/M	Busness	5 years	22/09/2017	31/10/2017	38	52	90	Good
9.	2959	Suppiramaniyan	69/M	Cooley	10 years	02/11/2017	25/11/2017	23	72	95	Moderate
10.	3167	Eswaran	65/M	Painter	5 years	03/12/2017	26/12/2017	23	71	94	Moderate
11.	3174	Thangasamy	60/M	Cooley	6 years	04/12/2017	24/12/2017	20	72	92	Good
12.	106	Thiruneelakandar	70/M	Cooley	5 years	19/01/2018	05/02/2018	17	73	90	Moderate
13.	115	Rajakopal	70/M	Cooley	6 years	19/01/2018	26/01/2018	37	53	90	Good
14.	112	Vellammal	66/F	Housewife	3 years	19/01/2018	04/02/2018	15	76	91	Moderate
15.	122	Serthu	67/M	Milk man	4 years	20/01/2018	05/02/2018	15	78	93	Good
16.	130	Muththaiya	70/M	Carepentar	10 years	21/01/2018	05/02/2018	14	76	90	Good
17.	271	Ranjitham	47/F	Cooley	3 years	02/02/2018	16/03/2018	42	50	92	Good
18.	308	Vellaiyammal	63/F	Housewife	5 years	06/02/2018	23/02/2018	17	75	92	Good
19.	426	Saraswathy	60/F	Housewife	3 years	17/02/2018	20/03/2013	33	60	93	Good
20.	1157	Rathasubbulaxmi	54/F	Beedi maker	6 years	28/04/2018	15/05/2018	17	53	70	Moderate

INVESTIGATION CHART FOR OUT-PATIENT: BLOOD INVESTIGATIONS & MMRC DYSPNEA SCALE SCORE

Sl. No.	OP No.	BEFORE TREATMENT					MMRC Dyspnea Scale Score	AFTER TREATMENT					MMRC Dyspnea Scale Score
		Hb	TC	DC				Hb	TC	DC			
				P	L	E				P	L	E	
1.	32101	13	9300	62	33	05	4	13.1	9000	64	32	04	3
2.	37549	12.6	9000	64	34	02	2	12.4	8300	64	34	02	0
3.	40810	12	8000	62	36	02	3	12.5	8100	63	35	02	1
4.	40847	11.5	6400	60	36	03	4	13	7300	61	26	03	1
5.	52651	12.9	6400	64	32	04	4	13	7200	65	32	03	3
6.	58024	15.2	10100	70	25	05	3	11.8	8000	65	33	02	2
7.	59223	11.3	8000	50	47	03	3	10.3	8600	68	28	04	1
8.	59746	12.8	7600	65	31	04	3	12.9	7700	66	33	01	2
9.	61703	12.8	8000	65	29	06	2	12	8000	64	30	06	2
10.	63884	10.0	6500	54	40	06	3	10.1	6800	63	36	03	0
11.	66783	9.3	6800	67	29	04	2	10	7100	63	35	02	0
12.	71009	11	8700	51	40	09	3	12	8000	65	31	04	1
13.	71838	10.5	5500	50	45	05	3	11.6	7200	66	32	02	2
14.	71949	9.6	8100	55	40	05	3	10	8300	68	30	02	2
15.	74507	9.5	9800	59	30	11	4	9.7	9600	62	33	05	3
16.	75203	11	7500	57	40	03	2	10.8	8000	59	37	04	0
17.	76426	12.5	7000	62	34	04	3	13	7000	63	33	04	1
18.	76581	12	8800	68	29	05	2	12.3	8500	66	30	04	0
19.	82948	12	9800	62	30	08	3	11.8	8900	64	31	05	1
20.	85387	11.2	8000	55	40	05	2	11.5	8400	65	28	07	1

Hb-Hameoglobin, TC- Total White Cell Count, DC- Differential Count White Cell Count, P-Polymorph, L-Lymphocyte, E-Eusinophil

INVESTIGATION CHART FOR IN-PATIENT: BLOOD INVESTIGATIONS & MMRC DYSPNEA SCALE SCORE

Sl. No.	IP No.	BEFORE TREATMENT					MMRC Dyspnea Scale Score	AFTER TREATMENT					MMRC Dyspnea Scale Score
		Hb	TC	DC				Hb	TC	DC			
				P	L	E				P	L	E	
1.	1135	10.8	8000	66	28	06	3	11.1	6500	60	34	06	1
2.	1737	14.7	7000	55	40	04	3	14	7200	60	38	02	2
3.	1779	10.3	6800	58	38	04	3	10.6	7000	60	38	02	3
4.	1871	13.9	9600	55.3	31.6	03	2	11.7	7000	62	38	00	0
5.	1957	10.1	8000	58	36	06	3	10.5	7800	60	37	03	1
6.	2234	10.5	8800	64	34	06	2	9.9	7800	64	32	04	0
7.	2441	14.7	7000	55	40	04	4	14.0	7200	60	38	02	3
8.	2612	11	9100	54	44	04	2	12.0	9500	60	33	07	1
9.	2959	12	8600	60	24	16	4	12.4	8100	60	36	04	3
10.	3167	11.5	8100	60	35	05	2	12.2	8100	60	38	02	0
11.	3174	10.9	8200	60	35	05	3	10	8000	62	36	02	1
12.	106	10.8	9200	69	16	15	4	11.6	7500	70	20	10	3
13.	115	12.1	9800	70	26	04	3	12.0	8900	68	28	04	1
14.	112	11	9100	54	44	02	4	12.0	9500	60	33	07	3
15.	122	10.4	9900	80	15	05	2	12.5	9000	70	26	04	1
16.	130	11.1	6000	62	34	04	3	12	7000	60	34	06	1
17.	271	12	8000	62	36	02	3	12.5	8000	62	36	02	1
18.	308	12.8	6500	61	35	04	3	13.8	6500	60	36	04	0
19.	426	12	8600	60	24	16	3	12.4	8100	60	36	04	1
20.	1157	15	9000	58	38	04	3	13.2	7200	65	33	02	2

Hb-Hameoglobin, TC- Total White Cell Count, DC- Differential Count White Cell Count, P-Polymorph, L-Lymphocyte, E-Eusinophil

INVESTIGATION CHART FOR OUT-PATIENT: PATIENTS BLOOD SUGAR & URINE SUGAR

Sl. No.	OP No.	BLOOD TEST						URINE TEST					
		BEFORE TREATMENT			AFTER TREATMENT			BEFORE TREATMENT			AFTER TREATMENT		
		FBS	PPBS	S.U	FBS	PPBS	S.U	ALB	SUGAR	DEPOSITS	ALB	SUGAR	DEPOSITS
1.	32101	180	255	35	150	225	31	Nil	+++	NAD	Nil	++	NAD
2.	37549	165	242	33	110	153	30	Nil	++	NAD	Nil	+	NAD
3.	40810	145	220	26	100	143	26	Nil	Nil	NAD	Nil	Nil	NAD
4.	40847	160	235	19	121	202	20	Nil	+	NAD	Nil	Nil	NAD
5.	52651	291	315	30	280	300	29	Nil	+++	NAD	Nil	+++	NAD
6.	58024	150	225	25	140	223	25	Nil	Nil	NAD	Nil	Nil	NAD
7.	59223	170	248	23	105	148	23	Nil	Nil	NAD	Nil	Nil	NAD
8.	59746	240	290	28	200	270	27	Nil	++	Pus cells ++	Nil	++	NAD
9.	61703	260	308	28	240	290	28	Nil	++	Pus cells ++	Nil	Nil	NAD
10.	63884	185	260	33	152	165	30	Nil	++	NAD	Nil	Nil	NAD
11	66783	168	243	28	120	201	27	Nil	++	Pus cells ++	Nil	Nil	NAD
12.	71009	148	225	22	110	138	21	Nil	Nil	NAD	Nil	Nil	NAD
13.	71838	160	235	33	150	215	31	Nil	Nill	Pus cells +++	Nil	Nill	Pus cells +
14.	71949	162	238	34	132	208	32	Nil	Nill	Pus cells +++	Nil	Nil	Pus cells +
15.	74507	189	268	21	140	220	20	Nil	+++	NAD	Nil	++	NAD
16.	75203	160	235	29	112	143	28	Nil	++	NAD	Nil	+	NAD
17.	76426	172	253	30	124	151	29	Nil	+	NAD	Nil	Nil	NAD
18.	76581	136	220	29	110	134	28	Nil	Nill	NAD	Nil	Nil	NAD
19.	82948	160	240	31	115	145	30	Nil	Nil	NAD	Nil	Nil	NAD
20.	85387	143	223	30	98	139	29	Nil	Nil	NAD	Nil	Nil	NAD

FBS-Fasting Blood Sugar, PPBS-Post Parandial Blood Sugar, S.U-Serum Urea, ALB-Albumin

INVESTIGATION CHART FOR IN-PATIENT: PATIENTS BLOOD SUGAR & URINE SUGAR

Sl. No.	IP No.	BLOOD TEST						URINE TEST					
		BEFORE TREATMENT			AFTER TREATMENT			BEFORE TREATMENT			AFTER TREATMENT		
		FBS	PPBS	S.U	FBS	PPBS	S.U	ALB	SUGAR	DEPOSITS	ALB	SUGAR	DEPOSITS
1.	1135	165	238	26	115	148	26	Nil	+	Pus cells ++	Nil	Nil	Nil
2.	1737	152	226	25	142	221	25	Nil	Nil	Nil	Nil	Nil	Nil
3.	1779	227	301	35	180	165	34	Nil	+++	Nil	Nil	Nil	Nil
4.	1871	136	214	28	95	135	27	Nil	Nil	Nil	Nil	Nil	Nil
5.	1957	175	250	27	150	224	26	Nil	+	Pus cells ++	Nil	Nil	Nil
6.	2234	160	235	26	122	203	25	Nil	+	Nil	Nil	+	Nil
7.	2441	178	252	30	135	205	29	Nil	+	Nil	Nil	Nil	Nil
8.	2612	162	242	34	117	147	33	Nil	++	Pus cells ++	Nil	++	Nil
9.	2959	159	236	24	149	224	23	Nil	+	Nil	Nil	Nil	Nil
10.	3167	175	254	22	145	220	21	Nil	++	Pus cells ++	Nil	+	Pus cells ++
11.	3174	167	242	30	121	203	29	Nil	++	Pus cells ++	Nil	+	Nil
12.	106	160	235	23	152	227	23	Nil	+	Nil	Nil	Nil	Nil
13.	115	159	232	26	121	202	26	Nil	+	Pus cells ++	Nil	+	Pus cells ++
14.	112	225	298	28	176	256	28	Nil	++	Pus cells ++	Nil	Nil	Nil
15.	122	175	254	28	125	152	27	Nil	+	Nil	Nil	Nil	Nil
16.	130	145	224	27	110	139	27	+	+	5-7 pus cells	Nil	Nil	Nil
17.	271	136	210	22	85	123	21	Nil	Nil	Nil	Nil	Nil	Nil
18.	308	140	220	28	110	139	28	Nil	+	Nil	Nil	Nil	Nil
19.	426	155	230	26	120	148	25	Nil	+	Pus cells ++	Nil	Nil	Nil
20.	1157	170	245	27	143	224	27	Nil	+	Nil	Nil	+	Nil

FBS-Fasting Blood Sugar, PPBS-Post Parandial Blood Sugar, S.U-Serum Urea, ALB-Albumin

INVESTIGATION CHART FOR OUT-PATIENT: PATIENTS HbA1C & LIPID PROFILE

Sl. No.	OP No.	BEFORE TREATMENT						AFTER TREATMENT					
		HbA1C	LIPID PROFILE					HbA1C	LIPID PROFILE				
			TC	HDL	LDL	VLDL	TGL		TC	HDL	LDL	VLDL	TGL
1.	32101	7.9	240	58	158	46	232	6.9	223	36	140	47	236
2.	37549	7.4	234	34	148	49	246	6.4	187	46	140	50	260
3.	40810	6.7	191	37	130	23	118	6.1	180	32	135	20	80
4.	40847	7.3	175	48	103	24	170	5.9	181	52	96	26	120
5.	52651	11.9	213	30	68	95	475	11.3	223	57	91	80	398
6.	58024	6.9	119	53	37	29	143	6.5	155	67	50	21	105
7.	59223	7.6	208	42	130	36	180	6.4	192	51	95	46	228
8.	59746	10	236	60	144	32	161	8.7	211	65	121	25	127
9.	61703	10.6	206	31	186	12	190	10	185	31	136	12	60
10.	63884	8.1	239	67	138	34	168	6.2	213	66	120	25	140
11.	66783	7.5	247	57	170	20	98	6.3	210	50	180	18	88
12.	71009	6.8	270	52	196	22	110	5.9	240	42	152	20	121
13.	71838	7.3	168	51	96	21	105	6.9	170	53	92	25	120
14.	71949	7.3	173	48	103	24	170	6.4	181	52	96	26	120
15.	74507	8.2	176	58	194	35	167	6.8	189	59	102	33	173
16.	75203	6.8	265	38	198	25	172	5.5	240	35	135	24	151
17.	76426	6.7	226	39	136	52	260	5.9	210	68	120	22	110
18.	76581	6.4	186	60	107	21	105	5	200	61	93	28	98
19.	82948	7.2	251	39	174	39	198	5.6	205	67	109	21	105
20.	85387	6.6	196	39	127	23	118	5	192	50	122	20	102

TC-Total Cholesterol, HDL-High Density Lipoprotein, LDL-Low Density Lipoprotein, TGL-Triglyceride

INVESTIGATION CHART FOR IN-PATIENT: LIPID PROFILE

Sl. No.	IP No.	BEFORE TREATMENT						AFTER TREATMENT					
		HbA1C	LIPID PROFILE					HbA1C	LIPID PROFILE				
			TC	HDL	LDL	VLDL	TGL		TC	HDL	LDL	VLDL	TGL
1.	1135	7.4	244	34	161	49	246	6.2	167	66	46	55	273
2.	1737	7	196	39	127	23	118	6.6	192	50	122	20	102
3.	1779	9.6	201	53	126	22	112	8.2	210	58	102	25	138
4.	1871	6.5	278	38	119	21	105	5	192	46	102	28	120
5.	1957	7.7	255	72	150	33	151	6.9	240	80	130	30	148
6.	2234	7.3	230	54	152	24	178	6.2	230	54	132	34	118
7.	2441	7.8	190	39	117	23	392	6.3	192	50	122	20	102
8.	2612	6.8	182	48	98	30	176	5.6	175	58	93	25	113
9.	2959	7.2	226	30	117	78	392	6.8	154	40	84	30	115
10.	3167	7.7	240	58	236	46	232	6.6	223	36	140	47	236
11.	3174	6.9	227	39	136	52	260	5.8	215	46	146	23	75
12.	106	7.3	191	37	129	24	118	7	180	30	137	13	67
13.	115	6.8	175	48	103	24	170	5.8	181	52	96	26	120
14.	112	9.5	270	50	150	20	180	8.2	208	48	106	17	186
15.	122	7.2	275	35	123	17	87.1	6.2	163	72	66	25	127
16.	130	6.7	230	54	152	24	178	5	168	46	88	34	171
17.	271	6.5	227	61	142	23	118	4.7	200	44	128	27	157
18.	308	6.5	205	57	119	29	145	5	201	54	97	17	98
19.	426	7.1	218	41	118	58	293	5.7	181	50	150	31	186
20.	1157	7.6	181	50	150	31	186	6.6	154	40	84	30	150

TC-Total Cholesterol, HDL-High Density Lipoprotein, LDL-Low Density Lipoprotein, TGL-Triglyceride

BMI CHART FOR OUT-PATIENTS (OP)

Sl. No.	OP No.	Name	Age / Sex	BMI					
				Before Treatment			After Treatment		
				WT	HT	BMI	WT	HT	BMI
1.	32101	Shangar	65/M	80	165	29.4	76	165	27.9
2.	37549	Muththu	63/M	54	153	23.1	48	153	20.5
3.	40810	Ramapandiyan	65/M	72	151	31.5	65	151	28.5
4.	40847	Balasunthari	55/F	83	161	32	76	161	29.3
5.	52651	Kanthavel	48/M	86	171	29.4	84	171	28.7
6.	58024	Perumal	73/M	70	165	25.7	68	165	24.9
7.	59223	Ganthimathy	61/F	84	165	30.9	76	165	27.9
8.	59746	Suriyakala	48/F	66	154	27.8	60	154	25.3
9.	61703	Suppammal	61/F	86	160	33.6	85	160	33.2
10.	63884	Thagira	40/F	65	149	29.3	58	149	26.1
11.	66783	Muththulaxmi	48/F	65	165	23.9	53	165	19.5
12.	71009	Rajinidevi	56/F	60	147	27.8	54	147	24.9
13.	71838	Pazanisamy	64/M	72	164	26.8	70	164	26.0
14.	71949	Peshimuththu	60/M	85	179	26.5	82	179	25.6
15.	74507	Mani	61/F	54	152	23.4	54	152	23.4
16.	75203	Vasantha	55/F	58	152	25.1	52	152	22.5
17.	76426	Seenivashan	51/M	72	162	27.4	63	162	24.0
18.	76581	Manommani	60/F	58	152	25.1	54	152	23.4
19.	82948	Chanthanakumar	52/M	74	160	28.9	66	160	25.8
20.	85387	Sangarammal	56/F	79	149	35.6	74	149	33.3

WT-Weight, HT-Height, BMI-Body Mass Index

BMI CHART FOR IN-PATIENTS (IP)

Sl. No.	OP No.	Name	Age / Sex	BMI					
				Before Treatment			After Treatment		
				WT	HT	BMI	WT	HT	BMI
1.	1135	Rajam	60/F	79	149	35.6	72	149	32.4
2.	1737	Sangaran	70/M	80	162	30.4	75	162	28.5
3.	1779	Thangaraj	65/M	65	165	23.9	64	165	23.5
4.	1871	Pisshumani	59/M	65	153	27.7	59	153	25.2
5.	1957	Thaivakambar	71/M	50	150	22.2	49	150	21.8
6.	2234	Shangar	70/M	80	165	29.0	72	165	26.4
7.	2441	Thurairaj	65/M	80	165	29.4	75	165	27.5
8.	2612	Akpar	70/M	78	168	27.6	70	168	24.8
9.	2959	Suppiramaniyan	69/M	73	158	29.2	68	151	27.2
10.	3167	Eswaran	65/M	65	154	27.4	62	154	26.1
11.	3174	Thangasamy	60/M	88	172	29.7	80	172	27.0
12.	106	Thiruneelakandar	70/M	80	168	28.3	78	168	26.9
13.	115	Rajakopal	70/M	64	154	26.9	56	154	23.6
14.	112	Vellammal	66/F	77	150	34.2	76	150	33.7
15.	122	Serthu	67/M	72	151	31.5	66	151	28.0
16.	130	Muththaiya	70/M	65	154	27.4	60	154	25.2
17.	271	Ranjitham	47/F	68	154	28.7	60	154	25.3
18.	308	Vellaiyammal	63/F	76	158	30.4	68	158	27.2
19.	426	Saraswathy	60/F	85	160	33.2	75	160	28.0
20.	1157	Rathasubbulaxmi	54/F	65	154	27.4	61	154	25.7

WT-Weight, HT-Height, BMI-Body Mass Index

PULMONERY FUNCTION TEST FOR OUT-PATIENTS (OP) & IN-PATIENTS (IP)

S.No	Patients Name	Before Treatment					After Treatment				
		Parameters	Pred	M.PRE	% Pred	PFT Report	Parameters	Pred	M.PRE	% Pred	PFT Report
1.	Mr.Perumal 73/M Wt:70 Ht:165	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.74 1.94 70.80 2.36 7.34	1.53 1.33 86.93 1.31 4.94	56 69 123 56 67	Early Small Airway Obstruction Moderate Restriction	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.55 2.00 78.43 2.36 6.63	2.76 2.24 81.16 2.31 3.48	108 112 103 86 52	Early Small Airway Obstruction Spirometry within Normal Limits
2.	Mrs.Rajinidev 56/F Wt: 60 Ht: 147	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	1.87 1.42 75.94 1.79 5.00	1.57 1.00 63.69 00.79 1.16	84 70 84 44 23	Early Small Airway Obstruction Moderate Obstruction	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.35 1.77 75.32 2.81 7.01	1.73 1.73 100 4.12 4.85	74 98 133 147 69	Early Small Airway Obstruction Mild Restriction Test within Normal Limits
3	Mrs.Ganthimathy 61/F Wt:84 Ht: 165	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.50 1.86 74.40 2.06 5.83	1.14 1.14 100.00 01.24 1.56	46 61 134 60 27	Early Small Airway Obstruction Moderate Obstruction	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.69 1.90 70.63 2.34 7.27	2.12 1.55 73.11 1.28 2.30	79 82 104 55 32	Early Small Airway Obstruction Mild Restriction Test within Normal Limits
4.	Mr.Thurairaj 65/M Wt: 80 Ht: 165	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.28 1.82 81.7 6.58 2.27	1.75 0.88 50.30 00.58 0.27	77 48 65 29 22	Early Small Airway Obstruction Moderate Obstruction	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.25 1.80 81.6 6.55 2.23	2.03 1.04 51.20 02.66 0.51	90 58 63 41 23	Early Small Airway Obstruction Moderate Obstruction
5.	Mr.Serthu 67/M Wt: 72 Ht: 151	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	3.07 2.26 73.62 2.72 7.79	00.84 00.84 100.00 00.87 2.40	27 37 136 32 30	Early Small Airway Obstruction Severe Obstruction	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.22 1.67 75.23 2.31 6.07	1.89 1.44 76.19 01.13 3.79	85 86 101 49 262	Early Small Airway Obstruction Spirometry within Normal Limits

6.	Mrs.Muththulaxmi48/F Wt: 65 Ht: 165	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.52 2.12 84.4 5.69 2.79	2.19 1.75 79.90 5.48 1.63	87 83 95 96 58	Early Small Airway Obstruction Severe Obstruction	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.52 2.12 84.4 5.69 2.79	2.46 1.84 74.80 5.71 1.43	98 87 89 100 61	Early Small Airway Obstruction Mild Obstruction
7.	Mrs.Suriyakala 48/F Wt: 66 Ht: 154	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.52 2.16 86.7 5.74 2.95	1.32 0.69 52.30 1.14 043	52 32 60 20 15	Early Small Airway Obstruction Severe Obstruction	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.52 2.16 86.7 5.74 2.95	1.73 1.06 61.30 1.79 074	69 49 71 31 25	Early Small Airway Obstruction Moderate Obstruction
8.	Mrs.Thagira 40/F Wt: 65 Ht: 149	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	3.82 3.21 84.9 8.62 4.03	3.10 2.80 88.60 4.96 3.33	83 87 104 58 83	Early Small Airway Obstruction Moderate Restriction	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.35 1.77 75.32 2.81 7.01	1.73 1.73 100.00 4.12 4.85	74 98 133 147 69	Early Small Airway Obstruction Mild Restriction Test within Normal Limits
9.	Mr. Shangar 70/M Wt: 80 Ht: 165	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.22 1.60 72.07 2.00 5.96	2.36 00.47 19.92 00.35 01.95	106 29 28 18 33	Early Small Airway Obstruction Severe Obstruction Very Severe stage	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.22 1.60 72.07 2.00 5.96	2.36 00.47 19.92 00.35 01.95	106 29 28 18 33	Early Small Airway Obstruction Severe Obstruction Very Severe stage
10.	Mr. Thangaraj 68/M Wt: 65 Ht: 165	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.81 2.04 72.60 2.58 7.52	1.28 00.50 39.06 00.43 00.58	46 25 54 17 08	Early Small Airway Obstruction Mixed Blockage Very Severe stage	FVC L FEV 1 L FEV1/FVC % FEF 25-75 L/s PEFR L/s	2.81 2.04 72.60 2.58 7.52	1.28 00.50 39.06 00.43 00.58	46 25 54 17 08	Early Small Airway Obstruction Mixed Blockage Very Severe stage

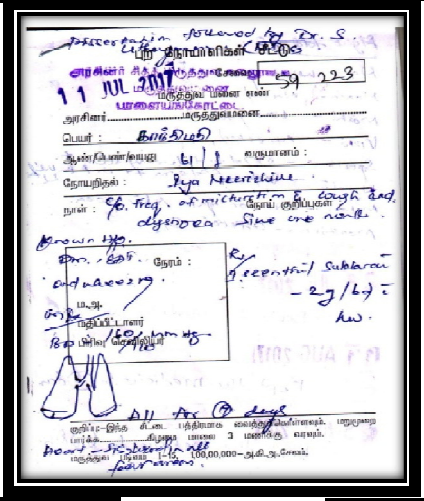
PULMONERY FUNCTION TEST REPORT BEFORE TREATMENT, AFTER TREATMENT

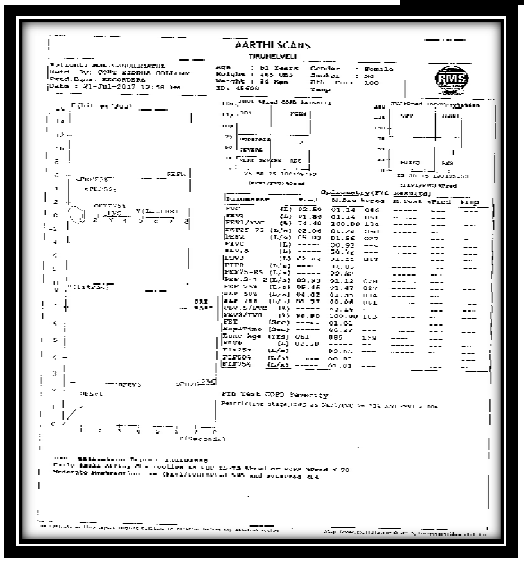
S.No	Patients Name	Parameters	Predected	BT	AT
1.	Mr.Perumal 73/M Wt:70 Ht:165	FVC L	2.74	56%	108%
		FEV 1 L	1.94	69%	112%
		FEV1/FVC %	70.80	123%	103%
		FEF 25-75 L/s	2.36	56%	86%
		PEFR L/s	7.34	67%	52%
2.	Mrs.Rajinidev 56/F Wt: 60 Ht: 147	FVC L	1.87	84%	74%
		FEV 1 L	1.42	70%	98%
		FEV1/FVC %	75.94	84%	133%
		FEF 25-75 L/s	1.79	44%	147%
		PEFR L/s	5.00	23%	69%
3	Mrs.Ganthimathy 61/F Wt:84 Ht: 165	FVC L	2.50	46%	79%
		FEV 1 L	1.86	61%	82%
		FEV1/FVC %	74.40	134%	104%
		FEF 25-75 L/s	2.06	60%	55%
		PEFR L/s	5.83	27%	32%
4.	Mr.Thurairaj 65/M Wt: 80 Ht: 165	FVC L	2.28	77%	90%
		FEV 1 L	1.82	48%	58%
		FEV1/FVC %	81.7	65%	63%
		FEF 25-75 L/s	6.58	29%	41%
		PEFR L/s	2.27	22%	23%
5.	Mr.Serthu 67/M Wt: 72 Ht: 151	FVC L	3.07	27%	85%
		FEV 1 L	2.26	37%	86%
		FEV1/FVC %	73.62	136%	101%
		FEF 25-75 L/s	2.72	32%	49%
		PEFR L/s	7.79	30%	262%
6.	Mrs.Muththulaxmi 48/F Wt: 65 Ht: 165	FVC L	2.52	87%	98%
		FEV 1 L	2.12	83%	87%
		FEV1/FVC %	84.4	95%	89%
		FEF 25-75 L/s	5.69	96%	100%
		PEFR L/s	2.79	58%	61%

7.	Mrs.Suriyakala 48/F Wt: 66 Ht: 154	FVC L	2.52	52%	69%
		FEV 1 L	2.16	32%	49%
		FEV1/FVC %	86.7	60%	71%
		FEF 25-75 L/s	5.74	20%	31%
		PEFR L/s	2.95	15%	25%
8.	Mrs.Thagira 40/F Wt: 65 Ht: 149	FVC L	3.82	83%	74%
		FEV 1 L	3.21	87%	98%
		FEV1/FVC %	84.9	104%	133%
		FEF 25-75 L/s	8.62	58%	147%
		PEFR L/s	4.03	83%	69%
9.	Mr. Shangar 70/M Wt: 80 Ht: 165	FVC L	2.22	106%	106%
		FEV 1 L	1.60	29%	29%
		FEV1/FVC %	72.07	28%	28%
		FEF 25-75 L/s	2.00	18%	18%
		PEFR L/s	5.96	33%	33%
10.	Mr. Thangaraj 68/M Wt: 65 Ht: 165	FVC L	2.81	46%	46%
		FEV 1 L	2.04	25%	25%
		FEV1/FVC %	72.60	54%	54%
		FEF 25-75 L/s	2.58	17%	17%
		PEFR L/s	7.52	08%	08%

Patient Name : GANTHIMANTHI (69Y/F)
OP No : 59223

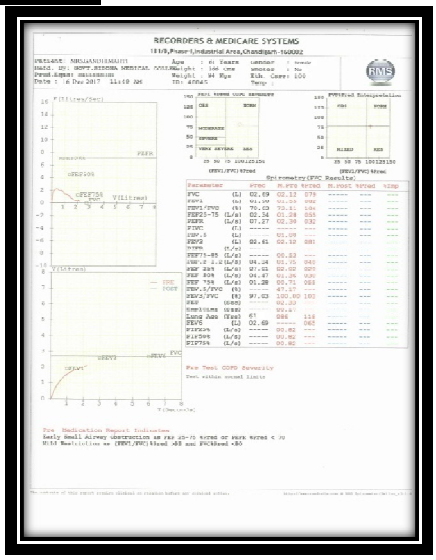
BEFORE TREATMENT





Patient Name : GANTHIMANTHI (69Y/F)
OP No : 59223

AFTER TREATMENT

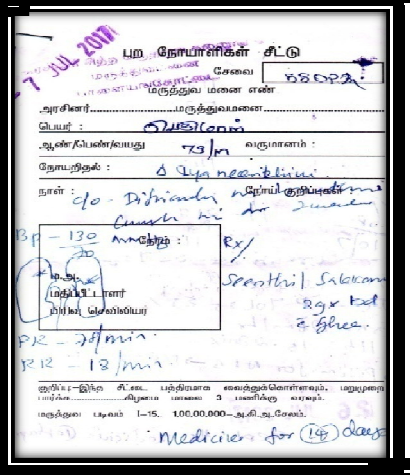


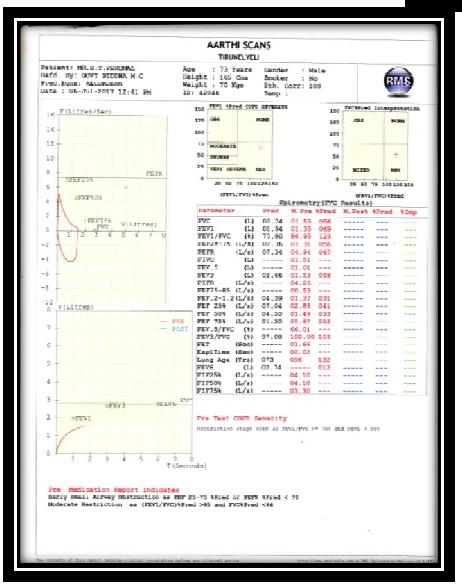
Patient Name : PERUMAL (73Y/M)
OP No : 58024
BEFORE TREATMENT

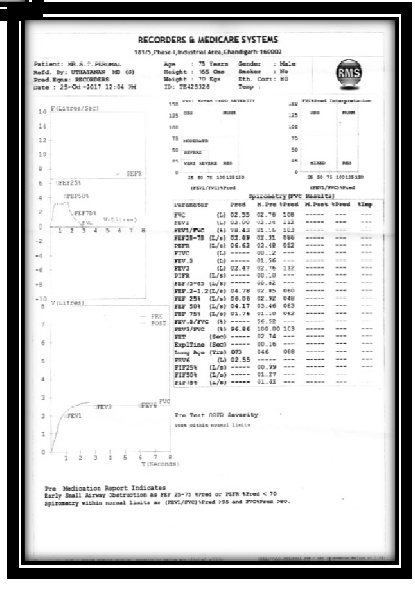

AARTHI SCANS & LABS
AN ISO 9001 ORGANISATION
Test Report
BIOCHEMISTRY
EDTA Blood Glycosylated HbA1c
End of the Report
SWAMINATHAN.K. MD.,
Pathologist

Patient Name : PERUMAL (73Y/M)
OP No : 58024
AFTER TREATMENT

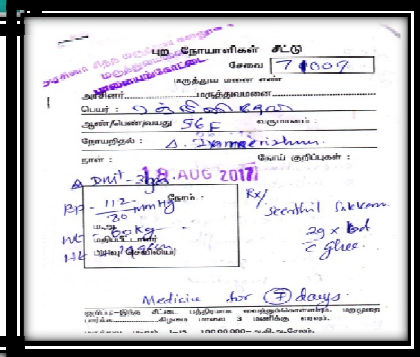

AARTHI SCANS & LABS
AN ISO 9001 ORGANISATION
Test Report
BIOCHEMISTRY
End of the Report
SWAMINATHAN.K. MD.,
Pathologist

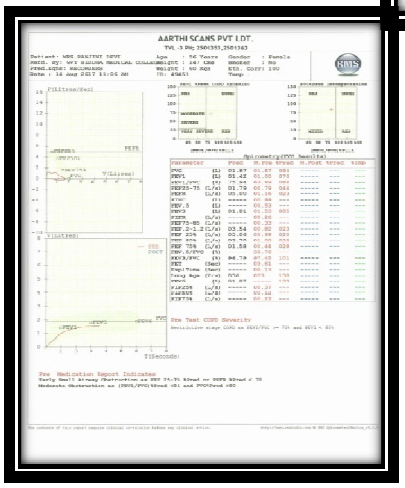

புற நோயாளிகள் சீட்டு
சேவை
மருத்துவ மனை எண்
மருத்துவமனை
பெயர் :
வயது/பெண்/ஆண் 73/m ஊராளாம் :
நோயாதல் :
நாள் :
Rx/
Medicines for (14) days


AARTHI SCANS
TIRUNELVELI
Spirometry(PFT Results)
Pre Test COPD Severity
Pre Medication Report Indicates

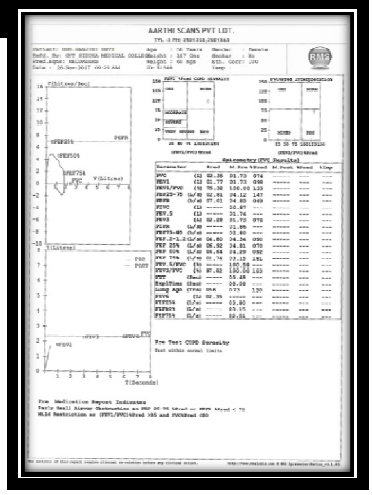

RECORDERS & MEDICARE SYSTEMS
Spirometry(PFT Results)
Pre Test COPD Severity
Pre Medication Report Indicates

Patient Name : RANJINIDEVI (56Y/F)
OP No : 71009
BEFORE TREATMENT





Patient Name : RANJINIDEVI (56Y/F)
OP No : 71009
AFTER TREATMENT



Patient Name : SERTHU (67Y/M)
IP No :

BEFORE TREATMENT

AARTHI SCANS & LABS

AN ISO 9001 ORGANISATION

SID No. : 16048846

Branch : TIRUNELVELI-VPI
Patient : SERTHU
Referrer : GOVT.SIDDHA MEDICAL COLLEGE

Age / Sex : 67 Y / Male
Reg. Date & Time : 19/04/2018 11:39
Result Date & Time : 22/04/2018 11:40
Report Date & Time : 22/04/2018 13:11

Page 1 of 1

Test Report

SPECIMEN	INVESTIGATION / METHOD	RESULT	UNITS	BIOLOGICAL REFERENCE INTERVAL
BIOCHEMISTRY				
EDTA Blood	Glycosylated HbA1c			
	HbA1c (HPLC)	7.6	%	Non-Diabetic Level: < 6 Goal : < 7 Unsatisfactory control:7.1-8.0 Action Suggested : > 8
	Mean Blood Glucose Level	173.47	mg/dl	

End of the Report

SWAMINATHAN.K. MD.,
Pathologist

The Aarthi Health Care Group - Elipudi - Vadapalani - Alwarpet - Tondarpet - Perambur - Perur - Tambaram - Velachery - Anna Nagar - Bengaluru

AFTER TREATMENT

AARTHI SCANS & LABS

AN ISO 9001 ORGANISATION

SID No. : 16049742

Branch : TIRUNELVELI-VPI
Patient : SERTHU
Referrer : GOVT.SIDDHA MEDICAL COLLEGE

Age / Sex : 67 Y / Male
Reg.Date & Time : 25/04/2018 11:40
Result Date & Time : 28/04/2018 11:48
Report Date & Time : 28/04/2018 13:11

Page 1 of 1

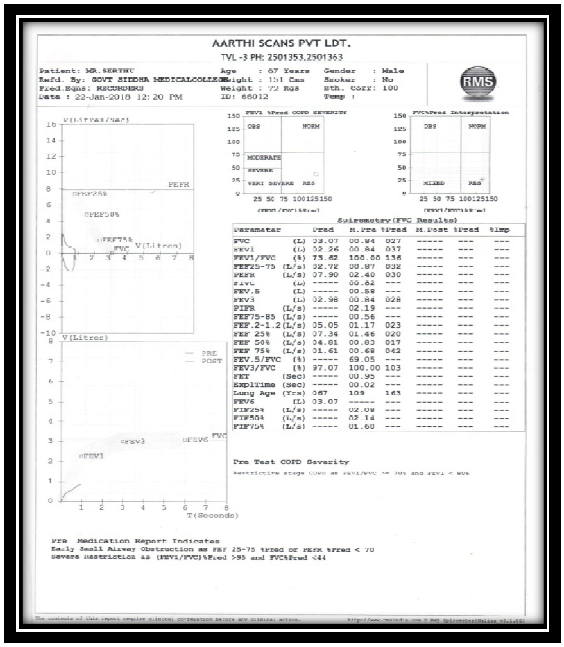
TEST REPORT

SPECIMEN	INVESTIGATION / METHOD	RESULT	UNITS	BIOLOGICAL REFERENCE INTERVAL
BIOCHEMISTRY				
EDTA Blood	Glycosylated HbA1c			
	HbA1c (HPLC)	7.0	%	Non-Diabetic Level: < 6 Goal : < 7 Unsatisfactory control:7.1-8.0 Action suggested : > 8
	Mean Blood Glucose Level	154.77	mg/dl	

End of the Report

SWAMINATHAN.K. MD.,
Pathologist

The Aarthi Health Care Group - Elipudi - Vadapalani - Alwarpet - Tondarpet - Perambur - Perur - Tambaram - Velachery - Anna Nagar - Bengaluru



AARTHI SCANS PVT LDT.

TVL-3 PH: 2501353,2501363

Patient: MR.SERTHU
Refd. By: GOVT SIDDHA MEDICALCOLLEGE
Pred.Eqns: RECORDERS
Date : 22-Jan-2018 12:20 PM

Age : 67 Years
Weight : 72 Kgs
ID: 66012

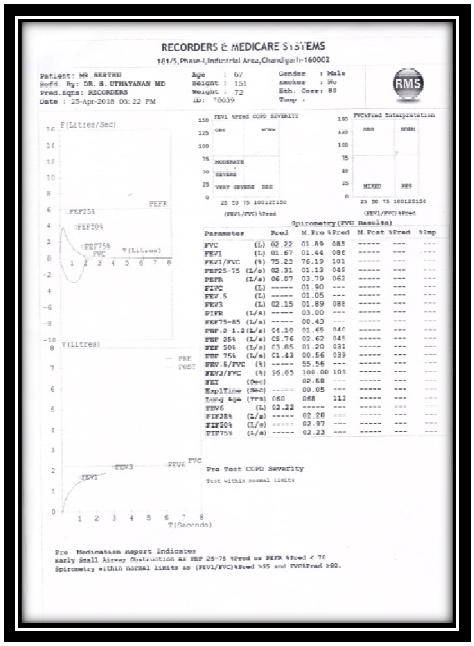
Gender : Male
Smoker : No
Eth. Corr: 100
Temp :

Spirometry(FVC Results)

Parameter	Unit	M.Pre %Pred	M.Post %Pred	%Imp
FVC	(L)	03.07	00.84	027
FEV1	(L)	02.26	00.84	037
FEV1/FVC	(%)	75.62	100.00	132
FEF25-75	(L/s)	02.72	00.87	032
PEFR	(L/s)	07.90	02.40	030
FIVC	(L)	-----	00.82	---
FEV.5	(L)	-----	00.58	---
FEV3	(L)	02.98	00.84	028
PIFR	(L/s)	-----	02.19	---
FEF75-85	(L/s)	-----	00.56	---
FEF.2-1.2	(L/s)	05.05	01.17	023
FEF 25%	(L/s)	07.36	01.46	020
FEF 50%	(L/s)	04.01	00.83	017
FEF 75%	(L/s)	01.61	00.68	042
FEV.5/FVC	(%)	-----	69.05	---
FEV3/FVC	(%)	97.07	100.00	103
FET	(Sec)	-----	00.95	---
Explitime	(Sec)	-----	00.02	---
Lung Age	(Yrs)	067	109	163
FIVC6	(L)	03.07	-----	---
FIV0.5	(L/s)	-----	02.08	---
FIF50%	(L/s)	-----	03.14	---
FIF75%	(L/s)	-----	01.60	---

Pre Test COPD Severity

PFR Medication Report Indicates
Early Small Airway Obstruction as FEF 25-75 %Pred or PEFR %Pred < 70
Severe Restriction as (FEV1/FVC)%Pred >95 and FVC%Pred <44



RECORDERS & MEDICARE SYSTEMS

161/5, Phase-I, Industrial Area, Chandigarh-160002

Patient: MR SERTHU
Refd. By: DR. S. UTHAYANAN MS
Pred.Eqns: RECORDERS
Date : 25-Apr-2018 09:22 PM

Age : 67
Height : 151
Weight : 72
ID: 76039

Gender : Male
Smoker : No
Eth. Corr: 80
Temp :

Spirometry(FVC Results)

Parameter	Pred	M.Pre %Pred	M.Post %Pred	%Imp
FVC	(L)	02.22	01.86	083
FEV1	(L)	01.67	01.44	086
FEV1/FVC	(%)	75.23	76.19	101
FEF25-75	(L/s)	02.31	01.13	048
PEFR	(L/s)	06.87	03.79	055
FIVC	(L)	-----	01.90	---
FEV.5	(L)	-----	01.05	---
FEV3	(L)	02.15	01.89	088
PIFR	(L/s)	-----	03.00	---
FEF75-85	(L/s)	-----	00.43	---
FEF.2-1.2	(L/s)	04.30	01.45	047
FEF 25%	(L/s)	05.76	02.62	045
FEF 50%	(L/s)	03.65	01.20	032
FEF 75%	(L/s)	01.42	00.56	039
FEV.5/FVC	(%)	-----	55.56	---
FEV3/FVC	(%)	96.05	100.00	103
FET	(Sec)	-----	02.68	---
Explitime	(Sec)	-----	00.05	---
Lung Age	(Yrs)	060	068	113
FIVC6	(L)	02.22	-----	---
FIF25%	(L/s)	-----	02.28	---
FIF50%	(L/s)	-----	02.97	---
FIF75%	(L/s)	-----	02.23	---

Pre Test COPD Severity

Test within normal limits

Pre Mechanism Report Indicates
early Small Airway Obstruction as FEF 25-75 %Pred or PEFR %Pred < 70
Spirometry within normal limits as (FEV1/FVC)%Pred >95 and FVC%Pred >80.

Discussion

CHAPTER-V

DISCUSSION

The Iya Neerizhivu refers to Diabetes associated with COPD which leads to increases the risks of Respiratory complications. Uncontrolled long standing diabetes is the main cause for developing the diabetic complications. This clinical study is designed to target the risks of Respiratory complications ensuing diabetes and to improve the quality of living of the diabetic individuals, with an efficacious herbal formulation mentioned in Siddha literature. In this study, 40 type-II diabetic patients attending the OP and IP at the Dept. of Pothu Maruthuvam, Govt. Siddha Medical College and Hospital, Palayamkottai were randomly selected for the study. 20 screened and selected patients were admitted as in in patients in Department of Pothu Maruthuvam and were treated with the trial medicine. After discharge all the twenty patients were followed as the Out patients. 20 Out patients in the Out patients Department of Pothu Maruthuvam were also treated with the trial drug.The prognosis were closely monitored and recorded under the supervision of Professor, Reader and Assistant lecturer. The observations and result are discussed below.

1. Distribution of Gender

The subjects included males 50% in OP, 70% in IP and females 50% in OP and 30% in IP were affected proving gender disparity in the onset of the disease. The male population was more than the female counter part. This compares well with a study on WHO global data which stated that the prevalence ratio of diabetes between men and women varies markedly, with no consistent trend. The ADA stated the relative difference in frequency between the sexes is probably related to the presence of underlying factors, such as obesity, rather than to a sex-specific genetic tendency.

2. Distribution of Age

The highest incidence of Iya Neerizhivu is among the age group of 40-49 years, closely followed by 50-59 years. From this study, it was observed that the diabetic subjects were averagely older. This shows type-II diabetes begins typically in middle life or later, the prevalence rises with age.

3. Distribution of Educational Status

The assessment of patient's knowledge showed the majority of patients were middle and high school educated. The educational level had no impact on glycemic control, but the patients of high educational level had better awareness of the complications and a high rate of adherence to diet.

4. Distribution of Occupation

The highest incidence of Iya Neerizhivu is among OP and IP patients were coolie workers.it belong.

5. Distribution of Religion

The majority of patients were Hindus among OP 75% and IP 60%. The highest incidence is among the Hindu population, which is the major population in India. Diet and lifestyle of rituals may influence the control of blood sugar and COPD. It has been suggested that in spite of ethnic and cultural differences diabetics have significantly higher prevalence of COPD.

6. Distribution of Marital Status

The highest incidence among the OP and IP patients were married.

7. Distribution of Clinical Manifestation

Diabetes is a chronic illness that requires continuing medical care and patient self-management education to prevent acute complications and to reduce the risk of long-term complications. The data from the observation showed majority of incidence of polyuria, polydipsia, nocturia, in both In patients and out-patients.

COPD itself usually causes symptoms like Coughing, Sputum, Dyspnea, Wheezing, and Expectoration of sputum etc., these features also present among OP & IP patients in relative percentages who were recruited in the study.

8. Distribution of Mode of Onset

The onset of Iya Neerizhivu ensues a chronic mode of onset with relative percentage of 65% in OP and 85% in IP. The percentage of recently found supports the fact that in many diabetics the disease is first detected when the patient presents with a complication.

9. Distribution of Duration of Illness

Iya Neerizhivu is greatly noticed in 40 patients suffering with about more than 3 years to 6 years suffering with Neerizhivu. It was observed that duration of type-II diabetes had a positive correlation with glycated haemoglobin. This is because the body becomes more resistant to insulin with increasing duration of diabetes. Various studies

are proved that the amount of carbohydrate attached to the HbA1C increases with increasing duration of the disease.

10. Distribution of Family History

Among the Out patients, 60% of the patients had positive family history and 40% of the patients had negative family history in in patients 40% had negative family history. Family history is high prevalence to get diabetic complications.

11. Distribution of Previous Treatment

Among OP and IP patients of 100% were taken previous therapy. Majority of patients despite of previous therapy for Neerizhivu had developed Iya Neerizhivu, reflecting the resistance developed to the undertaken therapy.

12. Distribution of Personal History

The observations illustrate that the disease was majority of patients were taken mixed diet. According *Yugi Vaidhya Chinthamani*, the dietary factors that cause the disease are taking excessive consumption of non-vegetarian diet. Here the observations coincide with Yugi's concept.

Although regulation of blood glucose and PFT to achieve near normal levels is a primary goal in the management of diabetes and COPD, and thus, dietary techniques that limit hyperglycaemia following a meal are important in limiting the complications of diabetes.

Among the Out patients 20% & 50% of the patients were alcoholics and smokers, Among In patients 25% & 70% of the patients also were alcoholics and smokers. Above the patients in OP and IP observed poor control of blood sugar.

Though smoking has a hand in the incidence of Iya Neerizhivu, it was noted that patients with no such habits also reported with the above condition.

13. Distribution of Socio economic Status

Among the Out-patients 25% belonged to the lower middle Socio-Economic status and 15% belonged to lower middle and poor group.

This Observation indicates no class variation in the manifestation of the disease. But the low income should influence the awareness of diet, health care and routine medical check-up of patients.

14. Distribution of Other System Involvement

Both in patients, Out Patients had central nervous system, cardiovascular system and musculo skeletal system affected. Among this majority of cases affected with

musculo skeletal system in OP and IP patients. The course may be due to obesity and degenerative changes.

15. Body Mass Index

According to WHO 60% of the quality of an individual's health depends on his / her diet and regimens. Early adoptions of healthy habits can problems of future years. Present study reflected that there was a higher prevalence of overweight and obesity among OP and IP patients (60% & 60%). Subjects with higher HbA1C levels also had significantly higher measurements in BMI and waist circumference and hip circumference as compared with those of desirable HbA1C levels.

16. Distribution of Constitution of Body

Among, 40 Out patients and In patients 95% were thontha thegi and the present study reflected that higher prevalence was kapham combined with other doshas.

17. Distribution of Gunam

100% of all the 40 patients included in the study had Rajogunam.

18. Distribution of Kaalam

The maximum numbers of cases were treated in their pitha kaalam among OP and IP patients. But in Siddha text denoted the Iyakaalam is more prevalence to Iya Neerizhivu.

19. Paruva Kaalam

There was high incidence of this study reflected Kaar kaalam (75%) among OP patients and Munpani kaalam (35%) among IP patients. The text book of Siddha maruthuvam stated elavenil and mudhuvenil kaalam. Therefore it could not counterpart of the disease origin.

20. Thinai

Among, out patients 90% belonged to Marutham (i.e. Plain & its surroundings) and 95% in In patients.The region where the study is conducted is Tirunelveli which belongs to the marutham thinai.

21. **Mukkutram**

a. Derangement of Vatham

Pranan, Viyanan, Uthanan , Samanan, Kirukaran and Devathathan were affected in all the 100% of the Out patients and In patients. Abanan was affected in 30% of the Out patients and 30% of the In patients. Koorman was affected in 10% of the Out patients and 20% of the in patients.

- Pranan maintains the life force in a normal healthy body, this vayu when affected causes difficulty in breathing, dyspnoea as presented along with Iya Neerizhivu .
- Abanan is responsible for excretion of urine and motion. This vayu is affected in this disease causing constipation and polyuria.
- Viyaanan functions to induce normal physiological movements in the body. This vayu is affected leading to decreased activity due to tiredness, claudication pain and weakness.
- Uthanan is responsible for upword motion, speech, strength of the mind and the body. Since there is a decrease in the expectoration, cough strength of the body and mind.
- Altered Samanan leads polyphagia and indigestion
- Koorman gives strength to the body and helps in vision; this vayu is affected in Iya Neerizhivu causing tiredness and a decreased vision due to aging.
- Kirukaran is responsible for appetite which is affected in this disease.
- Devathanthan is responsible for tiredness after sleep and emotion. In Iya Neerizhivu tiredness of body and soul occurs due to derangement of devathathan.

b. Derangement of Pitham

Analagam, Ranjagam and Sathagam were affected in 100% of both In patients and Out patients. Prasagam was affected in 60% of the Out patients and 35% of the In patients. Alosagam was affected in 5% of the Out patients and 25% of the In patients.

Analagam is responsible for appetite. Since there is excess appetite or loss of appetite among the patients.

- Ranjagam contributes to the normal function of the blood components.
- Sathagam enables the performance of the intended actions if altered causing tiredness.
- Prasagam gives lustre to the skin, which is affected also.
- Altered Alosagam causing blurring of vision.

c. Derangement of Kapham

In types of Kapha dosham, Avalambagam and Kilethagam were affected in all the 100% of both in patients and Out patients. Santhigam was affected in 65% of out patients and 75% of in patients.

- Avalambagam resides in the lungs and helps the other four types of kapham to function in equilibrium. Since the equilibrium is altered due to involvement of other forms of kapham also affected.

- Deranged Kiethagam excessive appetite or loss of appetite is present.
- Santhigam resides in the joints and helps in its movement. Since there was joint pain, it is affected which may be due to their aging or obesity.

22. Involvement of Ezhu Udalthathukkal

In ezhu udal Kattugal, Saaram and Senneer was affected in all 100% of the Out patients and In patients. Oon was affected in 65% of the Out patients and 75% of the In patients. Kozhuppu was affected in 80% of the Out patients and 85% of the In patients. Enbu was affected in 20% of the out-patients and of the 25% in patients and sukkilam was affected in 5% of out patients only.

- Saaram strengthens the body and mind, since, there is loss of appetite and strength less causing body tiredness the first thathu is affected.
- Senneer is affected which produces decreased haemoglobin. Oon is responsible for the structural muscular component of the body; this is affected in the weakness caused by stroke.
- Enbu and Kozhuppu are responsible for the movements of the body and gives lubrication to the joint cavities. There was reflected in masculo skeletal disorders like Oteo arthritis, back pain, shoulder pain etc…due to obesity, and senility.

23. Kanmenthiriyam

The present study showed kaal and eruvai were affected in majority of cases in OP and IP patients (50% & 25%).

24. Gnanenthiriyam

Among Out patients and In patients Mei was affected in 50% and 25% of the cases leads to altered sensation and pain in madhumegam due to altered Viyanan and Devathathan. The pathology also can be overlap with sign and symptoms of Iya Neerizhivu.

25. Kosam

Among 40 patients annamaya kosam (100%) was affected due to altered abanan, samana vayu, anaila Pitham and kilethagam, in udalkattukal saaram and senneer.

26. Envagai Thervugal

- Sparisam was affected in 50% of out patients and 25% of In patients due to altered sensations of pain in claudication and numbness in neuropathy.
- Niram was affected in 30% of out patients 35% of In patients due to loss of lustre.

- Vizhi was affected in 10% of out patients and 20% of in patients, blurring of vision due to cataract and aging.
- Malam was affected in 30% of out patients and in patients due to constipation.
- Naa and Moothiram were affected in in patients and out patients. There was presence of dryness of tongue due to dehydration and polyuria with excretion of albumin, glucose, and abnormal neerkuri.
- Mozhi was affected 10% among In patients only with Iya Neerizhivu in the study.
- In Naadi examination majority of cases had pitha vatha naadi in OP and IP patients (55% & 50%) Kapha vatham were 10% in OP and 30% in IP vatha pitham were 25% in OP and 20% in IP. Pitha Kapham and Kapha pitha naadi was not seen in Iya Neerizhivu.

27. Neerkuri

In Neerkuri, Niram was affected in 55% of Out-patients and 45% of In patients which the colour was replicated crystal clear urine and indicates asathiyam. Manam was affected like honey odour in 20% of out patients and 30% of In patients. Nurai was affected in 35% of out patients and 25% of In patients.

28. Neikuri

In Neikuri, 60% of out patients and 70% of In patients had Thontha neer. Which was reflected some Asathiya Neerkuri such features like conch shape, decoration type, bat shape, bow shape etc.

29. Laboratory Analysis

A. HbA1C

Among the 40 patients recruited for the study most patients in OP & IP (65% & 70%) had poor control (>8%) of HbA1C. Insulin affects the liver Apo-lipoprotein production. It regulates the enzymatic activity of Lipoprotein Lipase (LPL) and Cholesterol ester transport protein. All these factors are likely cause of copd in Diabetes mellitus. Moreover, insulin deficiency reduces the activity of hepatic lipase and several steps in the production of biologically active LPL may be altered in DM.

B. Pulmonary Function Test

As expected, those having diabetes were older, were more likely to be male, had a greater average BMI, and had a greater report of breathlessness and were more likely to have serious pulmonary exacerbations and pulmonary exacerbations more frequently if they had COPD. Those with diabetes had greater pack years of smoking 24 in 40 COPD subjects.

30. Gradation of results

Good response was found in 60% of out patients and 55% of in patients. Moderate improvement was found in 30% of out patients and in 40% of in patients. Poor result was found in 10% of out patients and 5% of the in patients. Bio statistical analysis showed significant difference in the action of the trial drug in lowering elevated blood sugar levels, HbA1C, total cholesterol, LDL, TGL, and HDL, PFT with a 'p' value of $p<0.001$ for blood sugar, $p< 0.001$ for HbA1C, $p<0.001$ for total cholesterol, $p<0.001$ for LDL $p<0.001$, for HDL $p<0.001$, for and TGL $p=0.001$ and PFT $p<0.001$, before and after treatment with the trial drug. The p value for VLDL cholesterol level was not statistically significant, although difference exists in their mean value with SD. It shows that though statistically significant clinically the trial drug had an effect in reducing the elevated Blood sugar, HbA1C, PFT. Anthropometric measurements also showed significant difference in the action of trial drug in lowering body weight, BMI and WHR with p value of <0.001

31. Microbiological Examination

Microbial test shows is highly sensitivity to both gram positive and gram negative bacteria. Escherichia coli 26mm/23mm, Proteus sp. 23mm/20mm, Staphylococcus aureus 23mm/20mm, Pseudomonas aeruginosa 22mm/21mm, Salmonella typhi 21 mm/19 mm

Summary

CHAPTER-VI

SUMMARY

The reported epidemiological data on the prevalence on diabetes, the expected increase in the population of diabetic individuals, the increased risk of respitary complications due to diabetes necessitate urgent preventive measures to be undertaken to manage the disorder.

Therefore in these clinical trial 40 patients with Iya Neerizhivu, of both sex and varying age groups were screened and selected as 20 in patients and 20 Out patients, to evaluate the efficacy of the trial drug in the management of Iya Neerizhivu.

The patients were subjected to investigations based on Siddha and modern parameters. The trial drug Seenthil Sakkarai was administered to all the selected patients, at a dose of 30 mg/kg BW three times a day before food, for a study period of 90 days.

Blood sugar (FBS, PPBS), HbA1C, lipid profile, PFT was recorded before and after treatment. Siddha diagnostic parameters of Naadi examination and neerkuri, nei kuri were also observed.

All the cases administered with the trial drug, they were not reported any adverse reactions. Few patients adapted to the medicine and recovered spontaneously, for such patients the textual dosage of the trial drug was followed. In those who had a persistent complaint, the dosage of the trial drug was titrated according to their Body Mass Index.

Significant improvement was observed in almost all the cases included in the study. Symptoms of tiredness, cough, dyspnoea, and expectoration were remarkably reduced. Significant decreases in the mean values of blood sugar levels, HbA1C, Lipid levels BMI, WHR, PFT were noted before and after treatment. For blood sugar and HbA1C the “p” value was $p<0.001$ and “p” value was $p<0.001$ and for total cholesterol “p” value was $p<0.001$, for LDL “p” value was $p<0.001$, for HDL “p” value was $p<0.001$, for TGL “p” value was $p<0.001$ for BMI ‘p’ value was <0.001, PFT “p” value was $p<0.001$ which implies that statistically the trial drug has Seenthil sakkarai is potent Anti-Hyperglycemic and Bronchodilator activates..

Conclusion

CHAPTER-VII

CONCLUSION

In this clinical study 60% of the patients showed good improvement, 30% showed moderate improvement and 10% showed poor improvement.

Clinically there was a significant decrease in the mean values of PFT along with blood sugar and HbA1C levels before and after treatment with Seenthil sakkarai.

Bio statistically the T2D and COPD, Bronchodilator activity of the trial drug is highly significant ('p' value of $p<0.001$ for blood sugar, $p<0.001$ for HbA1C, $p<0.001$ for PFT.

It can be concluded that Iya Neerizhivu can be well managed with the trial drug, Seenthil sakkarai which reduces blood sugar levels and HbA1C, a biochemical state desirable for the prevention of diabetes and its respiratory complications.

HbA1C can be used as a potential biomarker for predicting copd in type-II diabetic patients in addition to glycaemic control hence early diagnosis and may be utilized for screening high-risk diabetic patients for timely intervention with respiratory diseases (COPD).

Annexure

ANNEXURE-I

PREPARATION OF THE TRIAL DRUG

SEENTHIL SARKKARAI

Drugs:

Seenthil Sarkkarai

Purification and Preparation:

All the ingredients of these herbal formulations will purify according to the suitable procedure methods described in Siddha classical literature.

Cut and remove the outer covering of aged stem of Tinospora cordifolia will be shade dried and make into powder. Add 1400 ml water and knead well, then mix 5600ml water and allow precipitating. The flour of Tinospora Cordifolia will be precipitated in the latter. After filter the water and again add 5600 ml water into it and allow to precipitating. It will be done for 10 times. Then add kaadi neer mixed with lemon juice (16:1) allow to precipitating for one day. Like another day buttermilk and lemon juice (16:1) allow to precipitating. The ratio should be maintained to flour and solution is 1:4. Finally flour will be collected and dried.

Dose:

30 mg/ Kg/BW/daily three times a day.

Adjuvant:

Ghee.

Uses:

Mega Disorders, Diabetes, Diseases Of Urinary Tract, Internal Hemorrhages, Intermittent Fevers, Chronic Fevers , Diarrhea, Dysentery, Bilious Disease Due To Hyper Acidity, Poisonous Bites, Persistent Cough, Asthma, Jaundice, Indigestion, Helminthiasis, Gonorrhea, Inflammations And Allergy, General Debility

PROPERTIES OF INDIVIDUAL DRUGS

rejy- ***Tinospora cordifolia.***

Synonym :mkuj tyy› Nrhk tyy› mkui j› mkuj fnfhb› F z ly

Botanical name : *Tinospora cordifolia*

Family : Menispermaceae

Parts used : leave, Stem, Root

Part used in trial drug : Stem (Seenthil Maa)

Siddha properties:

- Siddha Name : Seenthil
- Suvai : Kaippu (Bitter)
- Thanmai : Veppam (Hot)
- Pirivu : Karppu (Pungent)

Pharmacological actions:

Anti–Periodic, Bronchodilator, Alternative, Diuretic, Anti Diabetic, Anti-microbial actions, Demulcent.

Phytochemical constituents:

Bitter glucoside giloin, Giloinin, Gilo-sterol, Columbin, Chasmanthin, Palmarin, Tinosporon, Tinosporic acid, Berberine.

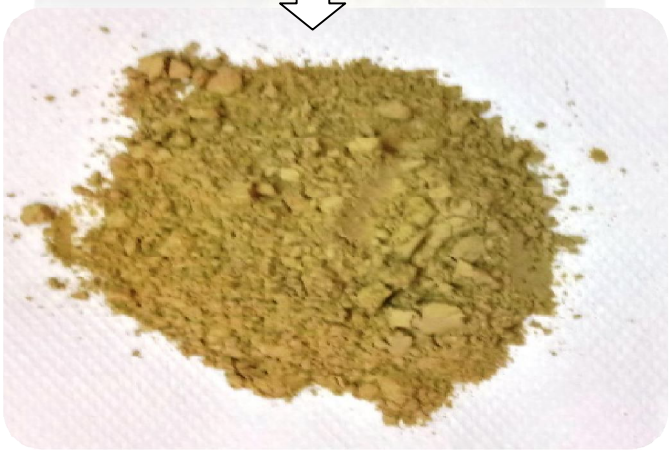
nghJ f F z k:

,qF ngUejhfk vdGUff ujjg jjk
XqFk kJNkf Klb z kNghk-Xqf t su
$ejy KbkhNj $WQrQ rt naDQ
rejy rUff iua d ru.
(g.F.t gf.v z -360)
Fllk gjn dlLk FQrujj d Nwhwnrhw Aq
fllk ngu jhq faNehAk-gllTld
nrejKd gQnrdNt rej Yg Nghl i sej
jejh tseufFr rhk (Njud nt z gh)
(F z ghlk ghfk 1- gf.v z 456)

Therapeutic Uses in Siddha:

Diabetes, Persistent Cough, Asthma, Inflammations and Allergy, Intermittent Fevers, Chronic Fevers.

rejþy r f f i u



ANNEXURE-II

BIO CHEMICAL ANALYSIS OF "SEENTHIL SARKKARAI" PREPARATION OF THE EXTRACT

The extract is directly prepared from the trial drug Seenthil Sarkkarai.

Preparation of the Extract:

5g of the drug was weight accurately and placed in a 20ml of distilled water is added and dissolved well. Then it's boiled well for about 10 minutes. It is coiled and filtered in a 100ml volumetric flask and then it is made to 100ml with distilled water. This fluid is taken for analysis.

QUALITATIVE ANALYSIS

Sl. No.	EXPERIMENT	OBSERVATION	INFERENCE
1.	**TEST FOR CALCIUM** 2ml of the above prepared extract is taken in a clean test tube. To this add 2ml of 4% Ammonium oxalate solution.	A white precipitate is formed.	Indicates the presence of Calcium**.**
2.	**TEST FOR SULPHATE:** 2ml of the extract is added to 5% Barium chloride solution.	A white precipitate is formed	Indicates the presence of Sulphate.
3.	**TEST FOR CHLORIDE** The extract is treated with Silver nitrate solution.	No white precipitate is formed.	Absence of chloride.
4.	**TEST FOR CARBONATE** The substance is treated with concentrated Hcl.	No brisk effervescence is formed.	Absence of Carbonate.
5.	**TEST FOR STARCH** The extract is added with weak Iodine solution.	Blue colour is formed.	Indicates the presence of Starch.
6	**TEST FOR FERRIC IRON** The extract is acidified with Glacial acetic acid and Potassium ferro cyanide.	No blue colour is formed.	Absence of ferric Iron
7.	**TEST OF FERROUS IRON** The extract is treated with concentrated Nitric acid and Ammonium thio cynaate solution.	Blood red colour is formed.	Indicates the presence of Frrous Iron.
8.	**TEST FOR PHOSPHATE** The extract is treated with Ammonium molybdate and concentrated Nitric acid.	No yellow precipitate is formed.	Absence of phosphate.

9.	**TEST FOR ALBUMIN** The extract is treated with Esbach's reagent.	No yellow precipitate is formed.	Absence of albumin.
10.	**TEST FOR TANNIC ACID** The extract is treated with Ferric choloride.	No Blue black precipitate is formed.	Absence of Tannic acid**.**

Sl. No.	EXPERIMENT	OBSERVATION	INFERENCE
11.	**TEST FOR UNSATURATION** Potassium permanganate solution is added to the extract.	It gets decolourised.	Indicates the presence of unsaturated compound**.**
12.	**TEST FOR THE REDUCING SUGAR** 5ml of Benedict's qualitative solution is taken in a test tube and allowed to boil for 2 mts and added 8-10 drops of the extract and again boil it for 2 mts.	No Colour change occurs.	Absence of reducing sugar**.**
13.	**TEST FOR AMINO ACID** One or two drops of the extract is placed on a filter paper and dried it well. After drying, 1% Ninnydrin is sprayed over the same and dried it well.	Violet colour is formed.	Indicates the presence of Amino acid**.**
14.	**TEST FOR ZINC:** The extract is treated with Potassium Ferrocyanide.	No white precipitate is formed.	Absence of Zinc.

INFERENCE: Calcium, Sulphate, Frrous Iron, unsaturated compound, and amino acid are present in Seenthil Sarkkarai.

ANNEXURE-III (A)

ANTI-HYPERGLYCEMIC EFFECT OF SEENDHIL SARKKARAI IN EXPERIMENTAL DIABETES AND THEIR EFFECTS ON KEY METABOLIC ENZYMES INVOLVED IN CARBOHYDRATE METABOLISM

INTRODUCTION

Diabetes mellitus is a metabolic disorder in which the body does not produce or properly utilize insulin. It causes disturbance in carbohydrate, protein and lipid metabolism and complications such as retinopathy, micro angiopathy and nephropathy. In practical terms, diabetes mellitus is a condition in diabetes, a profound alteration in the concentration and composition of lipid occurs. The global figure of people with diabetes set rise from the current estimate of 150-220 million in 2010 and 300 million in 2025.

Despite the immense strides that have been made in the understanding and management of diabetes the disease and disease related complications are increasing unabated. In spite of the presence of known anti-diabetic medicine in the pharmaceutical market, remedies from medicinal plant are used with success to treat this disease. Many traditional plants treatments for diabetes are used throughout the world and there is an increasing demand by patients to use the natural products with anti-diabetic activity.

The present investigation is undertaken to the study the effect of Seendhil Sarkkarai on changes in Body weight, Plasma glucose, Hemoglobin and glycosylated hemoglobin and lipid profile, metabolic enzymes and antioxidant enzymes levels.

EXPERIMENTAL MODELS

For the study of anti-diabetic an experimental model is selected in such a way that it would satisfy the following:

- The animal should develop hyperglycemia rapidly.
- Pathological changes in the site of induction should result from pancreatitis or damage of β-cells.
- The symptoms should be ameliorated or prevented by a drug treatment effective in human beings.

MATERIALS AND METHODS

Materials:

Animals : Male albino wistar rats (180-220gm)

Drugs : Seendhil Sarkkarai

Chemical : Streptozotocin (S. D Fine. Chem. Ltd, Mumbai)

Selection & acclimatization of animals:

Wistar strains of male albino rats weighing between 180-220gm are used for this study. The animals were housed in large spacious cages and they were fed with commercial pellets and access to water *ad libitum*. The animals were well acclimatized to the standard environmental condition of temperature ($22^0c \pm 5^0c$) and humidity (55 ±5%) and 12 hr light dark cycles throughout the experimental period.

INDUCTION OF DIABETES MELLITUS

Diabetes mellitus is induced in wistar rats by single intraperitoneal injection of freshly prepared solution of Streptozotocin (25mg/kg BW) in physiological saline after overnight fasting for 12hrs.[1]

Streptozotocin is commonly used to produce diabetes mellitus in experimental animals due to its ability to destroy the β-cells of pancreas possibly by generating the excess reactive oxygen species such as H_20_2, 0_2 and $H0^-$. The development of hyperglycemias in rats is confirmed by plasma glucose estimation 72 hrs post Streptozotocin injection. The rats with fasting plasma glucose level of >180-220mg/dl were used for this experiment.

Experimental procedure:

In the experiment a total of 30 rats (24 diabetic surviving rats & 6 normal rats) were used. Diabetes was induced in rats 3 days before starting the experiment. The rats were divided into 5 groups after the induction of Streptozotocin diabetes. In the experiment 6 rats were used in each group.

TREATMENT PROTOCOL

- Group-I: (Normal control) consist of normal rats given with 10ml/Kg of normal saline, orally.

- Group-II: (Toxic control) Diabetic control received 25mg/Kg of Streptozotocin through I.P.
- Group-III: Diabetic control received glipizide at a dose of (10mg/Kg orally) for 28 days.
- Group-IV: Diabetic control received Seendhil Sarkkarai at a dose of (100mg/Kg orally) for 28 days.
- Group-V: Diabetic control received Seendhil Sarkkarai at a dose of (200mg/Kg orally) for 28 days.

METHODOLOGY

Sample collection:

After 28 days of treatment, body weight, blood glucose, haemoglobin, glycosylated haemoglobin, plasma insulin, total cholesterol, triglycerides, HDL-cholesterol and phospholipids and glycogen content and antioxidant enzymes level were determined. Blood was collected from the eyes (venous pool) by sino-ocularpuncture. In EDTA coating plasma tubes for the estimation of blood parameters.

BIOCHEMICAL ANALYSIS

Estimation of blood glucose:

Blood glucose was estimated by commercially available glucose kit (One Touch Ultra) Johnson Johnson based on glucose oxidase method.

Plasma insulin:

Plasma insulin was determined by ELISA method using a Boehringer–Mannheim kit[4] with an ES300 Boehringer analyzer (Mannheim, Germany).

Estimation of total haemoglobin and glycosylated haemoglobin:

Total haemoglobin was determined by the method of Drabkin and Austin (1932) [5] and glycosylated haemoglobin was determined by the method of Sudhakar Nayak and Pattabiraman (1981).

Estimation of lipid & lipoprotein:

Plasma lipids were determined by auto analyzer according to the method of Parkeh and Jung (1970) (total cholesterol), Gidez and Webb (1950) (HDL-cholesterol), Zilversmith and Davis (1950) (phospholipids) and Rice (1970) (triglycerides).

Hepatic glucokinase and hexokinase activity

The part of liver for each test was perfused with ice cold 0.15M KCl and 1mM EDTA solution and homogenized twice its weight of ice cold buffer (0.01 cysteine and 1mM EDTA in 0.1 ml Tris-HCL, pH 7.4) and centrifuged for 20 min at 4^0C. Glucose phosphorylation was assayed by means of glucose 6 phosphate dependent spectrophotometric method (11)(Crane et al., 1955.

Glucose-6-phosphatase activity

The part of the liver for each test was homogenized with 40 times its weight of ice cold buffer (0.1 citrate-KOH, pH 6.5) and filtered through cheese cloth. Glucose-6-phosphatase activity was measured by phosphate release by the method Marjorie. The determination of phosphoric acid concentration in assay mixture was done calorimetrically (12) (Fiske et al., 1925).

Glycogen Content

The tissue sample was digested by hot concentrated 30% KOH and treated with anthrone reagent. Glycogen content was determined calorimetrically (Morales et al., 1973).

Statistical analysis:

The data for various biochemical parameters were analyzed using analysis of variance (ANOVA), and the group means were compared by Newman-Keul's multiple range test (NKMRT). Values were considered statistically significant at $p<0.01$.

Table No: 1

- **Effect of Seendhil Sarkkarai on initial and final body weight and blood glucose in normal and treated animals.**

GROUP	Body weight (g)		Blood glucose (mg / 100ml)	Blood glucose (mg / 100ml)
	Initial	Final	Initial	Final
G1	243 ± 6.15	245 ± 6.17	86.65 ± 4.40	88.85 ± 3.22
G2	233 ± 5.61	176 ± 7.33**[a]	85.28 ± 3.72	215.35 ± 5.81**[a]
G3	237 ± 7.53	241 ± 7.35	87.68 ± 4.33	121.50 ± 4.32*[b]
G4	233 ± 7.29	245 ± 7.32	86.78 ± 3.68	144.38 ± 7.23**[b]
G5	239 ± 7.39	243 ± 7.42	90.46 ± 3.85	153.45 ± 4.66**[b]

- Values are expressed as mean ± SEM.
- Values were compared by using analysis of variance (ANOVA) followed by Newman-Keul's multiple range tests.
- ** (a) Values are significantly different from normal control G1 at P<0.001.

  ** (b) Values are significantly different from Diabetic control G2 at P<0.01

Table No: 2

- **Effect of Seendhil Sarkkarai on plasma insulin, Hemoglobin & Glycosylated hemoglobin in normal and treated animals.**

GROUPS	Haemoglobin (gm/100ml)	Glycosylated Haemoglobin HbA1C (%)	Plasma Insulin (µU/ml)
G1	13.84 ± 1.62	0.45 ±0.07	37.24 ± 2.78
G2	6.50 ± 0.50**[a]	0.91 ±0.14**[a]	16.60 ± 1.63**[a]
G3	14.26 ± 1.47**[b]	0.46 ±0.06**[b]	35.35 ± 2.39**[b]
G4	12.41 ± 0.94**[b]	0.52 ±0.09**[b]	33.80 ±2.61**[b]
G5	12.60 ± 1.32**[b]	0.49 ±0.05**[b]	32.80 ± 2.63**[b]

- Values are expressed as mean ± SEM.
- Values were compared by using analysis of variance (ANOVA) followed by Newman-Keul's multiple range tests.
- ** (a) Values are significantly different from normal control G1 at P<0.001.

  ** (b) Values are significantly different from Diabetic control G2 at P<0.01.

Table No: 3

- **Serum lipids of Normal and experimental groups.**

GROUPS	Total Cholesterol (mg/dl)	Tri glyceride (mg/dl)	HDL-C (mg/dl)	Phospholipids (mg/dl)	LDL (mg/dl)
G1	85.74 ±2.64	94.46 ±2.68	56.46 ±1.84	127.45 ±2.42	19.30 ± 1.40
G2	225.42±7.46**[(a)]	158.60±4.55**[(a)]	36.68±1.34**[(a)]	219.44±6.32**[(a)]	44.65±2.52**[(a)]
G3	114.86±3.34**[(b)]	100.90±2.42**[(b)]	48.18 ±1.44	155.40 ±3.92	28.74±1.76**[(b)]
G4	125.54±3.58**[(b)]	120.70±2.90**[(b)]	44.43±1.42**[(b)]	164.60±4.12**[(b)]	34.25±1.54**[(b)]
G5	120.43±3.40**[(b)]	105.40±2.74**[(b)]	43.47±1.59**[(b)]	155.40±3.82**[(b)]	30.34±1.72**[(b)]

- Values are expressed as mean **±** SEM.
- Values were compared by using analysis of variance (ANOVA) followed by Newman-Keul's multiple range tests.
- ** (a) Values are significantly different from normal control G1 at P<0.001.
  ** (b) Values are significantly different from Diabetic control G2 at P<0.01.

Table No: 4

- **Effect of Seendhil Sarkkarai on glycogen content (mg/gm tissue)**

Groups	Liver Tissue Glycogen Content (mg/g tissue)
Group I	46.30 ± 3.50
Group II	14.24 ± 0.76*[a]
Group III	38.50 ± 1.78*[b]
Group IV	30.42 ± 1.30*[b]
Group V	32.64 ± 1.50*[b]

- Values are expressed as mean **±** SEM.
- Values were compared by using analysis of variance (ANOVA) followed by Newman-Keul's multiple range tests.
- ** (a) Values are significantly different from normal control G1 at P<0.001.
  ** (b) Values are significantly different from Diabetic control G2 at P<0.01.

Table No: 5

- **Effect of Seendhil Sarkkarai on enzymes involved in carbohydrate metabolism in rats**

Groups	Hexokinase (µg/mg)	Glucose-6-Phosphate (µg/mg)	Glucokinase (µg/mg)
Group I	0.216 ± 0.014	0.395 ± 0.010	29.42 ± 1.43
Group II	0.096 ± 0.004*[a]	0.132 ± 0.007*[a]	8.58 ± 0.35*[a]
Group III	0.132 ± 0.007*[b]	0.305 ± 0.010*[b]	21.22 ± 0.93*[b]
Group IV	0.127 ± 0.005*[b]	0.237 ± 0.007*[b]	18.15 ± 0.47*[b]
Group V	0.147 ± 0.006*[b]	0.246 ± 0.008*[b]	18.35 ± 0.96*[b]

- Values are expressed as mean ± SEM.
- Values were compared by using analysis of variance (ANOVA) followed by Newman-Keul's multiple range tests.
- ** (a) Values are significantly different from normal control G1 at P<0.001.
  ** (b) Values are significantly different from Diabetic control G2 at P<0.01.

Table No: 6

- **Effect of Seendhil Sarkkarai treatment on biochemical parameter I streptozotocin induced toxicity.**

Groups	SOD(U/mg) Protein	CATALASE (U/mg) Protein	GPX(U/mg) Protein	MOA(U/mg) Protein
Group I	132.24±2.41	292.42±2.40	1.23±0.07	3.94±0.18
Group II	*a69.23±1.44	*a191.88±2.73	*a0.47±0.02	*a7.46±0.16
Group III	*b119.10±2.80	*b261.44±1.90	*b0.92±0.02	*b5.54±0.13
Group IV	*b95.52±1.55	*b231.10±1.75	*b0.76±0.02	*b5.67±0.26
Group V	*b106.68±2.62	*b241.60±2.70	*b0.77±0.05	*b4.86±0.08

RESULTS

Table No: 1 illustrates the levels of initial and final blood glucose, and change in body weight, in normal rat, and treatment control animals in each group. The mean body weight of diabetic rats (G2) was significantly decreased as compared to normal control rats. The body weight of diabetic control rats treated with **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg was increased the body weight non-significantly as compared to normal control animals.

Fasting blood glucose level was significantly increased 218.45 ± 5.80 in diabetic animals as compared to normal animals. However the level of fasting blood glucose, returned to near normal range in diabetic rats treated with **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg.

Table No: 2 illustrate the levels of total hemoglobin, glycosylated hemoglobin and plasma insulin in normal rat and treatment control animals in each group.

The levels of total hemoglobin and plasma insulin levels were decreased significantly whereas glycosylated hemoglobin levels were increased significantly as compared to normal control rats. However the level of total hemoglobin, glycosylated hemoglobin and plasma insulin, returned to near normal range in diabetic rats treated with **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg.

Table No: 3 shows the level of serum total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL),Low density lipoprotein(LDL) and phospholipids of normal and experimental animals in each group.

Total cholesterol, triglycerides, high density lipoprotein, Low density lipoprotein (LDL) and phospholipids levels were significantly increased, where as HDL-C level was decreased in streptozotocin induced diabetic rats as compared to normal rats. Treatment of normal and streptozotocin induced diabetic rats with **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg for 28 days resulted in marked decrease in total cholesterol, triglycerides, Low density lipoprotein(LDL) and phospholipids levels and increase in HDL-C levels as compared to streptozotocin induced diabetic rats.

Effect of SEENDHIL SARKKARAI on Glycogen Content

Glycogen content of liver tissue was estimated on the 28^{th} day in non-diabetic control, diabetic control drug, treated group and positive control group as shown in Table **No: 4** in diabetic control rat liver glycogen content decreased significantly by 79.89 % as compared to non-diabetic control. Treatment with Glipizide, **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg led to 74.47 %, 66.05 % and 68.79% increase in liver glycogen content in comparison to diabetic control.

Effect of SEENDHIL SARKKARAI on Hepatic Enzymes

To establish diabetic, plasma glucose was determined 72hr after alloxan administration. Only those rats with over 180 mg% were included in the study. On the

28th day, hepatic enzymes Hexokinase, Glucokinase and substrate Glucose-6-phosphate were estimated in saline control (group I), diabetic control (group II) and treatment controls (groups III, IV and V).

The result has been compiled in **Table No: 5** As compared to non-diabetic control values, mean level of enzymes Hexokinase, Glucokinase and substrate Glucose-6-phosphate values decreased in diabetic control. The respective percentage decrease was 56.19%, 79.96% and 67.69% in diabetic control. Treatment with **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg for 28 days led to rise in percentage of these parameter by 22.03%, 56.03%, and 45.21% , 47.5%, 33.33% and 67.88% respectively ($P<0.001$) as compared to diabetic control. Also, treatment with Glipizide 10mg/kg for 28 days led to rise in percentage of these parameters by 27.55%, 65.39% and 58.0% respectively ($P< 0.001$) as compared to diabetic control.

In liver homogenate, there was significant decrease in SOD, CAT and GPx levels and increase in LPO levels were observed in animals treated with streptozocin 25mg/kg (group II) as compared to normal control group (Group I).

Pretreatment with **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg orally for 28 days increase the levels of above indices like SOD,CAT and GPx levels and decrease levels of LPO significantly ($P<0.01$) in group III, IV and V.

DISCUSSION

Streptozocin causes massive reduction in insulin release, through the destruction of β-cells of the islets of Langerhans. The mechanism of Streptozocin action was fully described elsewhere (Lazarow, 1964; Colca et al., 1983).[14,15] In our study, we have observed a significant increase in the plasma insulin level when Streptozocin induced diabetic rats were treated with **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg this could be due to potentiation of the insulin effect of plasma by increasing the pancreatic secretion of insulin from existing β- cells of islets of Langerhans or its release from bound insulin.

In uncontrolled or poorly controlled diabetes there is an increased glycosylation of a number of proteins including haemoglobin and α-crystalline of lens (Alberti and

Press, 1982). [16] Glycosylated haemoglobin (HbA1C) was found to increase in patients with diabetes mellitus to approximately 16% (Koenig et al., 1976) [17] and the amount of increase is directly proportional to the fasting blood glucose level (Jackson et al., 1979). [18] During diabetes the excess glucose present in blood reacts with haemoglobin. Therefore, the total haemoglobin level is decreased in Streptozocin induced diabetic rats (Sheela and Augusti, 1992).[19] Administration of **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg for 28 days prevents a significant elevation in glycosylated haemoglobin thereby increasing the level of total haemoglobin in diabetic rats. This could be due to the result of improved glycemic control produced by **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg.

The body weight was decreased in Streptozocin diabetic rats. **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg increases the body weight in Streptozocin induced diabetic rats. The ability of **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg to protect massive body weight loss seems to be due to its ability to reduce hyperglycemia.

The level of serum lipids are usually elevated in diabetes mellitus and such an elevation represents the risk of coronary heart disease (CHD). Lowering of serum lipids concentration through diet or drug therapy seems to be associated with a decrease in the risk of vascular disease. The abnormal high concentration of serum lipids in diabetic subject is mainly due to increased mobilization of free fatty acids from the peripheral fat depots, since insulin inhibits the hormone sensitive lipase. However, glucagon, catecholamines and other hormones enhance lipolysis. The marked hyperlipidaemia that characterized the diabetic state may therefore be regarded as a consequence of the uninhibited actions of lipolytic hormones on the fat depots.

In the Streptozocin -induced diabetes mellitus, the rise in blood glucose is accompanied by an increase in serum cholesterol and triglycerides. The levels of cholesterol and triglycerides and Low density lipoprotein (LDL) levels were brought to near normal by the treatment with **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg in Streptozocin induced diabetic rats.

The effect of **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg on diabetic hypertriglyceridemia could be through its control of hyperglycaemia. This is in agreement with the facts that:

1. The level of glycaemic control is the major determinant of total and very low density lipoprotein (VLDL), triglyceride, concentrations. Improved glycemic control following sulfonylurea therapy decreases the levels of serum VLDL and total triglycerides.The main 'anti-atherogenic' lipoprotein (HDL) is involved in the transport of cholesterol from peripheral tissues into liver and thereby it acts as a protective factor against coronary heart disease (CHD). The level of HDL-cholesterol was decreased in diabetic rats when compared with normal rats. [26] Our results clearly show that the level of HDL-cholesterol was increased in Streptozocin induced diabetic rats when treated with **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg. These results suggest that **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg has protective effect against Streptozocin induced diabetes and its complications.

   As reported earlier (Welihinda et al., 1986) in the current study also the liver glycogen content was reduced significantly in diabetic control as compared to non-diabetic control. Treatment with **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg prevented this alteration in glycogen content of liver tissue, but could not normalize the content of glycogen of the non-diabetic control. This prevention or depletion of glycogen in liver is possibly due to either stimulation of insulin release from β-cells [28] (Lolitkar et al., 1966) or due to the insulinomimetic activity of some components of the plants resulting in direct peripheral glucose uptake.

   Decreased enzymatic activity of Hexokinase, Glucokinase and substrate glucose-6- phosphate has been reported in diabetic animals resulting in depletion of liver and muscle glycogen**.** (Hikino et al., 1989) The present study also had similar results. Treatment with **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg significantly increased the hexokinase, Glucokinase activity and glucose-6-phosphate level in the liver, indicating an overall increase in glucose influx thus **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg seems to have an overall effect of increase in glucose utilization.

Oxidative stress is an imbalance between reactive oxygen species and the antioxidant defense mechanisms of a cell or tissue, which leads to lipid peroxidation, DNA damage, and the inactivation of many enzymes[30]. The enzymatic antioxidant defense system is the natural protector against lipid

peroxidation that includes superoxide dismutase, catalase and glutathione peroxidase. Reduced activities of these enzymes in the tissue of streptozotocin toxic rats were observed in our study. Superoxide dismutase protects against the superoxide radical (O2·−), which damages the membrane and its biological structure. Catalase primarily decomposes hydrogen peroxide to H_2O at a much faster rate, sharing this function with glutathione peroxidase. Glutathione peroxidase may play an important role in the removal of lipid hydroperoxides. The balance between these enzymes is important for the efficient removal of oxygen radicals from tissues[31] Therefore, reduction in the activity of these enzymes may result in a number of deleterious effects due to the accumulation of superoxide radicals and H_2O_2. Significant increases in the activities of these enzymes were observed on **Seendhil Sarkkarai** at a dose of 100mg/kg and 200mg/kg administration.

ANNEXURE –III (B)

ANTIHISTAMINIC AND ANTIANAPHYLACTIC ACTIVITY OF SIDDHA FORMULATION OF SEENDHIL SARKKARAI

Introduction

Allergy is one of the common diseases that affect mankind with diverse manifestations. The prevalence of allergy and asthma has risen in the recent years despite an improvement in the general health of the population. Allergic diseases are responsible for significant morbidity and have severe economic impact. Various epidemiological studies have identified the causes for an increase in the prevalence of upper and lower respiratory tract allergic diseases. Some of the postulated reasons are increasing environmental pollution and increased predisposition of individuals producing excessive IgE through a major change in the gene pool, changing lifestyles, and an increasing awareness of the disorders. Intensive research during the last several decades has highlighted the role of lymphocytes, immunoglobulins, mast cells, and various autacoids in the etiopathogenesis of allergic conditions. Inspite of the voluminous literature on the subject, the treatment of allergic diseases continues to be far from satisfactory. The available treatment options for upper and lower respiratory tract allergic diseases have major limitations owing to low efficacy, associated adverse events, and compliance issues.

AYUSH, an Indian system of medicine, has described several drugs from indigenous plant sources for use in the treatment of bronchial asthma and allergic disorders. In the present study, the effects of Siddha formulation of Seendhil Sarkkarai were studied on the active anaphylaxis and mast cell stabilization in rats, and histamine-induced bronchospasm in guinea pigs.

Materials and Methods

Animals

Inbred Wistar rats (175–200 g) and guinea pigs (400–600g) of either sex housed in standard conditions (temperature22 ± 2° C, relative humidity 60 ± 5% and 12 h light/dark cycle) were used. They were fed with standard pellet diet and water ad libitum. The Institutional Animal Ethics Committee approved the experimental protocol. Histamine and horse serum were procured from Sigma Chemicals and toluidine blue from

Loba-Chemie, Mumbai. Elisa kit for Ig_E was supplied by Orion diagnostics, Espoc, Finland. All other chemicals and reagents were procured from Hi-Media Laboratories limited, Mumbai.

Mast cell stabilizing activity

Treatment protocol

Twenty-four rats were divided into four groups of six animals in each group.

Group I Served as control and received vehicle (water).

Group II (Sensitized control group)

GroupIII Served as the treatment control, which was treated with Seendhil Sarkkarai at a dose of 100mg/kg body weight, in oral route.

GroupIV Served as the treatment control, which was treated with Seendhil Sarkkarai at a dose of 200 mg/kg body weight, in oral route.

In group11 to group 1V were sensitized by injecting 0.5 ml of horse serum subcutaneously along with 0.5 ml of triple antigen containing 20,000 million Bordetella pertussis organisms (Serum Institute of India Ltd.,Pune), Once a day for 14 days.

On day 14, the rats were sacrificed 2 h after the treatment and the intestinal mesentry was taken out for the study on mast cells. Mesentries along with intestinal pieces were excised and kept in Ringer Locke solution (NaCl 154, KCl 5.6, CaCl2 2.2, NaHCO3 6.0, glucose 5.55 mM/L of distilled water) at 37^{o}C. The mesenteric pieces were challenged with 5% horse serum for 10 min after which the mast cells were stained with 1.0% toluidine blue and examined microscopically for the number of intact and degranulated mast cells.[6]

Histamine-induced bronchospasm in guinea pigs

Bronchospasm was induced in guinea pigs by exposing them to 1% histamine aerosol under constant pressure (1 kg/cm2) in an aerosol chamber (24 × 14 × 24 cm) made of perplex

Glass,of the three groups of six animals each.

Group I served as control.

GroupII served as the treatment control, which was treated with Seendhil Sarkkarai at a dose of 100 mg/kg body weight, in oral route.

Group III served as the treatment control, which was treated with Seendhil Sarkkarai at a dose of 200 mg/kg body weight, in oral route.

The animals were exposed to 1% histamine aerosol under constant pressure (1 kg/cm2) in an aerosol chamber on day 0 without any treatment. The end point,preconvulsive dyspnea (PCD) was determined from the time of aerosol exposure to the onset of dyspnea leading to the appearance of convulsions.[7] As soon as PCD commenced, the animals were removed from the chamber and exposed to fresh air. This PCD was taken as day 0 value. On days 1 and 5,
2 h after the administration of the drug, the time for the onset of PCD was recorded as on day 0.

Statistical analysis

The results of various studies were expressed as mean ± SEM and analyzed statistically using one-way ANOVA, followed by Newmann keul's multiple range tests. $P<0.05$ was considered statistically significant.The analysis was performed using Graphpad Prism software package (Version 4.0).

RESULTS

Mast cell stabilizing potential of Seendhil SarkkaraiAntigen challenge resulted in significant degranulation of the mesentric mast cells. Pretreatment of sensitized animals with Seendhil Sarkkaraiat a dose of 100mg/kg and 200mg/kg, p.o., for 2 weeks resulted in a significant reduction in the number of disrupted mast cells ($P <0.001$) when challenged with horse serum.

Effect on Histamine-Induced Bronchospasm

Seendhil Sarkkarai at a dose of 100mg/kg and 200mg/kg p.o., significantly prolonged the latent period of PCD ($P <0.001$) as compared to control, following exposure to histamine aerosols on day 5 [Table no. 2].

Discussion

Experimental animal model of asthma is characterized by allergen-induced immediate airway constriction and late airway reactivity to a pharmacological vasoconstrictor such as histamine and leukotrienes. Histamine is a central mediator in the pathogenesis of allergic and inflammatory disorders. In the present study, Seendhil Sarkkarai prolonged the latent period of PCD in guinea pigs following histamine aerosol. This may be suggestive of an antihistaminic activity following treatment with Seendhil Sarkkarai.

Antigen challenge, in sensitized animals, results in the degranulation of mast cells, which is an important feature of anaphylaxis. In the present study, Seendhil Sarkkarai showed marked protection against the mast cell degranulation following antigen challenge in sensitized animals. Mast cell stabilizing activity of Seendhil Sarkkarai may be attributed to the presence of active constituents which are known for their mast cell stabilizing potential against antigen–antibody reaction and/or due to the suppression of IgE antibody production, which is responsible for degranulation mast cells.[8]

This antianaphylactic and antihistaminic effect may be caused by the stabilization of the mast cell membrane, suppression of IgE, and inhibition of pathological effects induced by the release of inflammatory mediators in Seendhil Sarkkarai treated animals. All the above findings lend credence to the beneficial use of Seendhil Sarkkarai in the treatment of asthma and related conditions.

However, further studies with other experimental models, especially to explore the role of cytokines are warranted to substantiate the antiasthmatic and antiallergic activity of Seendhil Sarkkarai.

TABLE NO: 1

EFFECT OF SEENDHIL SARKKARAI ON MAST CELL STABILIZATION IN SENSITIZED RATS

GROUPS	MAST CELLS	
	INTACT	DISRUPTED
Normal Control	85.50±3.48	15.90±0.86
Sensitized Rats	14.80±0.94	84.34±2.66
Seendhil Sarkkarai 100mg/kg	67.36±2.88*a	33.30±1.45*a
Seendhil Sarkkarai 200mg/kg	65.28±2.77*a	33.86±1.54*a

- Values are expressed as Mean±S.E.M

*a significantly different from sensitized control at $p<0.01$

TABLE NO: 2

EFFECT OF SEENDHIL SARKKARAI ON HISTAMINE INDUCED BRONCHOSPASM IN GUINEA PIGS.

GROUPS	PRE-CONVULSION DYSPNEA (PCD)(SEC)		
	DAY 0	DAY 1	DAY 5
GP 1	177.44±7.32	265.17±9.62	217.22±9.62
GP 2 (Seendhil Sarkkarai 100mg/kg)	184.17±6.42	225.23±6.53	415.23±13.11*a
GP3 (Seendhil Sarkkarai 200mg/kg)	185.42±6.32	227.30±8.41	410.13±12.32*a

Values are expressed as Mean ±S.E.M
*a significantly different from control on day 5 at $p<0.001$

ANNEXURE –III (C)

ANTI-INFLAMMATORY ACTIVITY OF SIDDHA FORMULATION OF SEENDHIL SARKKARAI

Introduction

Allergy is one of the common diseases that affect mankind with diverse manifestations. The prevalence of allergy and asthma has risen in the recent years despite an improvement in the general health of the population. Allergic diseases are responsible for significant morbidity and have severe economic impact. Various epidemiological studies have identified the causes for an increase in the prevalence of upper and lower respiratory tract allergic diseases. Some of the postulated reasons are increasing environmental pollution and increased predisposition of individuals producing excessive IgE through a major change in the gene pool, changing lifestyles, and an increasing awareness of the disorders. Intensive research during the last several decades has highlighted the role of lymphocytes, immunoglobulins, mast cells, and various autacoids in the etiopathogenesis of allergic conditions. Inspite of the voluminous literature on the subject, the treatment of allergic diseases continues to be far from satisfactory. The available treatment options for upper and lower respiratory tract allergic diseases have major limitations owing to low efficacy, associated adverse events, and compliance issues.

AYUSH, an Indian system of medicine, has described several drugs from indigenous plant sources for use in the treatment of bronchial asthma and allergic disorders. In the present study, the effects of Siddha formulation of Seendhil Sarkkarai were studied on the active anaphylaxis and mast cell stabilization in rats, and histamine-induced bronchospasm in guinea pigs.

Materials and Methods

Animals

Inbred Wistar rats (175–200 g) and guinea pigs (400–600g) of either sex housed in standard conditions (temperature22 ± 2° C, relative humidity 60 ± 5% and 12 h

The anti-inflammatory activities of siddha formulation **Seendhil Sarkkarai** at a dose of 100 and 200mg/kg were evaluated using carrageenan-induced paw edema method. The inflammation was readily produced in the form of edema with the help of irritant such as carrageenan. Carrageenan is a sulphated polysaccharide obtained from sea weed (Rhodophyceae) and when injected cause the release of prostaglandins by the way it produces inflammation and edema.

REQUIREMENTS:

Animal : Albino rat (180-200 g)

Drugs and chemicals : Carrageenan (1%w/v), Diclofenac sodium (standard), Carboxy methyl cellulose (1%w/v), Digital plethysmo meter. U G O Basile (Italy)

Test compounds : siddha formulation **Seendhil Sarkkarai**

METHOD:

Anti-inflammatory activity was performed by the following procedure of Bhandri et al (1) the animals were divided into 4 groups each having six animals. A freshly prepared suspension of carrageenan (1% w/v, 0.1 ml) was injected to the planter region of left hind paw of each rat. One group was kept as control and the animals of the other groups were pretreated with the siddha formulation **Seendhil Sarkkarai test** Compounds dissolved with 2 ml sterile water given through orally 30 min before the carrageenan treatment. The paw volumes of the test compounds, standard and control groups were measured at 60,240,360 minutes of carrageenan treatment with the help of Digital plethysmometer (Ugo basile, Italy). Mean increase in paw volume was measured and the percentage of inhibition was calculated.

% Anti-inflammatory activity = (Vc-Vt / Vc) x 100

Where, **Vt**-mean increase in paw volume in rats treated with test compounds,
Vc- mean increase in paw volume in control group of rats.

TABLE No: 1

ANTI-INFLAMMATORY ACTIVITY OF SIDDHA FORMULATION
SEENDHIL SARKKARAI

Treatment	Dose (mg/kg)	Paw volume(ml) as measuredby mercury displacement at 6 hour	Percentage inhibition of paw edema
Group I Normal saline	10ml/kg orally	5.62±0.96	-
Group II Std	10mg/kg I.P.Diclofenac sodium	1.77±0.43	72.36%*a
Group III Seendhil Sarkkarai	100mg/kg.Orally.	2.12±0.55	67.06%*a
Group IV Seendhil Sarkkarai	200mg/kg.Orally.	1.99±0.47	69.04%*a

* Data are expressed as Mean ± S.E.M.
* Data were analyzed by one way ANOVA followed by Newman's keul's multiple range tests, to determine the significance of the difference between the control group and rats treated with the test compounds.
* A Values were significantly different from normal control at P< 0.01.

Results

Anti- inflammatory activity

Both doses of siddha formulation **Seendhil Sarkkarai** at 100mg/kg and 200mg/kg were tested for their Anti- inflammatory activity by using carrageenan Induced rat paw edema method and the results are tabulated in table no 1. The results reveals that both doses of siddha formulation **Seendhil Sarkkarai** at 100mg/kg and 200mg/kg doses possesses significant Anti- inflammatory activity when compared to control group at p<0.01.

ANNEXURE –III (D)

ANALGESIC ACTIVITY OF SIDDHA FORMULATION OF SEENDHIL SARKKARAI

Introduction

Allergy is one of the common diseases that affect mankind with diverse manifestations. The prevalence of allergy and asthma has risen in the recent years despite an improvement in the general health of the population. Allergic diseases are responsible for significant morbidity and have severe economic impact.Various epidemiological studies have identified the causes for an increase in the prevalence of upper and lower respiratory tract allergic diseases. Some of the postulated reasons are increasing environmental pollution and increased predisposition of individuals producing excessive IgE through a major change in the gene pool, changing lifestyles, and an increasing awareness of the disorders. Intensive research during the last several decades has highlighted the role of lymphocytes, immunoglobulins, mast cells, and various autacoids in the etiopathogenesis of allergic conditions. Inspite of the voluminous literature on the subject, the treatment of allergic diseases continues to be far from satisfactory. The available treatment options for upper and lower respiratory tract allergic diseases have major limitations owing to low efficacy, associated adverse events, and compliance issues.

AYUSH, an Indian system of medicine, has described several drugs from indigenous plant sources for use in the treatment of bronchial asthma and allergic disorders. In the present study, the effects of Siddha formulation of Seendhil Sarkkarai were studied on the active anaphylaxis and mast cell stabilization in rats, and histamine-induced bronchospasm in guinea pigs.

Materials and Methods

Animals

Inbred Wistar rats (175–200 g) and guinea pigs (400–600g) of either sex housed in standard conditions (temperature22 ± 2° C, relative humidity 60 ± 5% and 12 h

ANALGESIC ACTIVITY

Analgesic activity of siddha formulation Seendhil Sarkkarai was evaluated by acetic acid induced writhing reflux in mice. Painful reaction in animals may be produced by the chemicals such as phenylquinone, bradykinin etc. Like that, acetic acid pain reaction which is characterized as a writhing response. Construction of abdomen, turning of trunk (twist) and extension of hind legs are taken as reaction to chemically induced pain. Analgesics (both narcotic and non-narcotic) inhibit writhing response.

REQUIREMENTS:

Animal : Swiss albino mice (20-25g) either sex

Drugs and chemicals : Diclofenac sodium (standard),

Acetic acid (1%v/v), Seendhil Sarkkarai

METHOD:

TREATMENT PROTOCOL

Group-1: Treated as normal control received 10ml/kg of normal saline through orally.

Group-2: Treated as Standard control received 10mg/kg of diclofenac sodium through Intraperitonealy.

Group-3: Treated as treatment control received 100mg/kg of Seendhil Sarkkarai administered through orally.

Group-4: Treated as treatment control received 200mg/kg of Seendhil Sarkkarai administered through orally.

Siddha formulation Seendhil Sarkkarai was administered one hour prior to the acetic acid administration. Note the onset on writhing. Record the numbers of abdominal contractions, trunk twist and extension of hind limbs as well as the number of animals showing such response during a period of 10 minutes were noted.

STATISTICS:

Data are expressed as mean ± SEM; data analyzed by one way ANOVA followed by Newman's keul's multiple range tests to determine the significance of the difference between the control group and rats treated with the extracts.

* Values were considered significant at P< 0.01.

TABLE No:1

ANALGESIC ACTIVITY OF SEENDHIL SARKKARAI BY ACETIC ACID INDUCED WRITHING REFLUX IN MICE

Treatment	Dose (mg/kg)	No. of writhing	% reduction in reaction time
Group I Normal saline	Inject 1%v/v acetic acid 1ml/100g of body weight	48.5±2.83	-
Group II Std	10mg/kg I.P.Diclofenac sodium	16.5±0.81	92.13%**
Group III Seendhil Sarkkarai	100mg/kg Administered through orally.	23.5±1.51	76.55%**
Group IV Seendhil Sarkkarai	200mg/kg Administered through orally	21.8±1.24	79.37%**

Values are expressed as mean±SEM

Values were find out by using one-way ANOVA followed by Newman's keuls multiple range tests.

** Values were considered significant at P< 0.01.

RESULTS

The table values show that analgesic activity of Seendhil Sarkkarai by acetic acid induced writhing reflex. The results reveals that both dose of Seendhil Sarkkarai possess significant analgesic activity at $p<0.01$.

ANNEXURE –III (E)

ANTIHISTAMINIC AND ANTIANAPHYLACTIC ACTIVITY OF SIDDHA FORMULATION OF SEENDHIL SARKKARAI

Introduction

Allergy is one of the common diseases that affect mankind with diverse manifestations. The prevalence of allergy and asthma has risen in the recent years despite an improvement in the general health of the population. Allergic diseases are responsible for significant morbidity and have severe economic impact. Various epidemiological studies have identified the causes for an increase in the prevalence of upper and lower respiratory tract allergic diseases. Some of the postulated reasons are increasing environmental pollution and increased predisposition of individuals producing excessive IgE through a major change in the gene pool, changing lifestyles, and an increasing awareness of the disorders. Intensive research during the last several decades has highlighted the role of lymphocytes, immunoglobulins, mast cells, and various autacoids in the etiopathogenesis of allergic conditions. Inspite of the voluminous literature on the subject, the treatment of allergic diseases continues to be far from satisfactory. The available treatment options for upper and lower respiratory tract allergic diseases have major limitations owing to low efficacy, associated adverse events, and compliance issues.

AYUSH, an Indian system of medicine, has described several drugs from indigenous plant sources for use in the treatment of bronchial asthma and allergic disorders. In the present study, the effects of Siddha formulation of Seendhil Sarkkarai were studied on the active anaphylaxis and mast cell stabilization in rats, and histamine-induced bronchospasm in guinea pigs.

Materials and Methods

Animals

Inbred Wistar rats (175–200 g) and guinea pigs (400–600g) of either sex housed in standard conditions (temperature22 ± 2° C, relative humidity 60 ± 5% and 12 h

ACUTE TOXICITY STUDY OF SEENDHIL SARKKARAI

Determination of acute oral toxicity is usually the initial screening step in the assessment and evaluation of the toxic characteristics of all compounds. The types of toxicity tests which are routinely performed by pharmaceutical manufacturers in the investigation of a new drug involve acute, sub-acute and chronic toxicity. Acute toxicity is involved in estimation of LD_{50} (the dose which has proved to be lethal (causing death) to 50% of the tested group of animals) (Shetty Akhila, *et al.,* 2007).(1)

Method: Acute oral toxicity of Seendhil Sarkkaraiis carried out as per the guidelines Organization of Economic Co-operation and Development (OECD) -423 guidelines after the animal ethical clearance from Institutional Animal Ethics Committee.

The albino mice are fasted overnight and provided only water, after which the **Seendhil Sarkkarai**is administered by gastric intubations to the relevant group of animals orally at the dose of 50 $mg.kg^{-1}$ body weight in Tween-80. The animals are then observed for 14 days and maintained with normal food. A mortality rate of 2 or 3 animals in 14 days is recorded and the dose is said to be toxic dose. But when mortality of one animal is observed, then the same dose is repeated again for confirmation. However, if mortality is not observed, the procedure is repeated for further higher doses such as 300 and 2,000 $mg.kg^{-1}$ body weight. Toxic symptoms are observed for 72 hrs including behavioral changes, locomotion, convulsions and mortality (Shah Ayub, 1997, Bürger, 2005). (2,3).

Cage Side Observations

Observations include changes in skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous systems, and somatomotor activity and behavior pattern. Special attention is directed for the observation of tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma.

Body Weight, Food and Water Intake

Body weight, food and water intake are recorded at two day intervals.

Pathology

Surviving animals are fasted overnight, weighed and humanely killed on the 15^{th} day using anesthetic ether. All test animals are subjected to gross necropsy.

SUBCHRONIC TEST FOR SEENTHIL SARKKARAI

This experiment evaluates the toxicity potential of Seenthil Sarkkarai.

Method: Male and female Wistar rats weighing 180 ± 10 g are used for the present study. The animals are divided into five groups of six animals each. The dose of the preparation is calculated based on the body weight of the animal. The animals in Group I are administered with a single daily dose of 0.5 ml of Tween 80 orally for 20 days. The animals in Group II are administered with 50 $mg.kg^{-1}$b.w. of the Seenthil Sarkkaraiorally once daily for 20 days. The animals in Group III are administered with 100 $mg.kg^{-1}$b.w. of the Seendhil Sarkkaraiorally once daily for 20 days. The animals in Group IV and V are administered once daily with 200 and 400 $mg.kg^{-1}$b.w. of the Seendhil Sarkkarairespectively for 20 days orally (Pieme,*et al* 2006, Joshi, *et al* 2007, Mythilypriya, *et al.*, 2007).(4,5,6)The animals are then weighed every five days, from the start of the treatment, to record the weight variation. At the end of the treatment, blood samples are collected by puncturing retro orbital plexus after mild anesthesia for biochemical analysis. The collected blood sample is centrifuged within 5 min of collection at 4000 g for 10 min to obtain plasma, which is analyzed for total cholesterol, total triglyceride, HDL-cholesterol levels,LDL-cholesterol,plasma glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine and urea.

RESULTS

ACUTE TOXICITY STUDY WITH SEENTHIL SARKKARAI

The acute toxicity of Seenthil Sarkkarai was evaluated using OECD-423 guidelines. There was no mortality or morbidity observed in animals through the 15 days period following single oral administration at all selected dose levels of the Seenthil Sarkkarai (Table-1). The animals did not show any changes in the general appearance during the observation period. Morphological characteristics such as fur, skin, eyes and nose appeared normal. No tremors, convulsion, salivation, diarrhea, lethargy or unusual behaviors such as self mutilation, walking backward and so forth were observed. Gait and posture, reactivity to handling or sensory stimuli, grip strength was also normal.

	Dose ($mg.kg^{-1}$)	Sign of Toxicity ($ST.\ NB^{-1}$)	Mortality ($D.S^{-1}$)
Group I	0	0/3	0/3
Group II	300	0/3	0/3
Group III	2000	0/3	3/3

Table 1.

Acute toxicity study of Seendhil Sarkkarai on experimental mice. The acute toxicity of Seendhil Sarkkarai on experimental mice was tested using OECD-423 guidelines, where ST- sign of toxicity; NB- normal behavior; D- died; S- survive. Values are expressed as number of animals (n=3).

Effect of Seendhil Sarkkarai in Subchronic Toxicity

Seenthil Sarkkarai was evaluated for subchronic toxicity.

Effect of Seendhil Sarkkarai on body weight changes in rats

The effect of Seenthil Sarkkarai was observed for their effect on the body weight changes from the study it was observed that, there was significant increase ($p<0.05$) in body weight in all the animals observed. The results are shown in Table.2.

Treatment	Day 1	Day 5	Day 10	Day 20
Control	179.19±5.4	180.40 ±6.12	189.10 ±6.30	189.6±6.30
Seenthil Sarkkarai **50 $mg.kg^{-1}$**	186.34 ±6.2	189.30 ±6.44	190.48 ±6.75	190.30±6.84*
Seenthil Sarkkarai **100 $mg.kg^{-1}$**	179.36 ±6.0	186.43 ±6.42	188.30 ±6.54	190.84±6.70*
Seenthil Sarkkarai **200 $mg.kg^{-1}$**	188.25 ±7.0	190.20±6.34	190.48 ±6.58**	198.35±6.72**
Seenthil Sarkkarai **400 $mg.kg^{-1}$**	179.54 ±6.34	186.35 ±6.65	188.15 ±6.65**	196.52±6.74**

Table.2

The effects of **Seendhil Sarkkarai** on body weight changes in rats. A study on the effects of **Seendhil Sarkkarai** on body weight changes in rats was carried out... where, group I animals (GPI) were treated with normal saline ($5ml.kg^{-1}$), group II animals (GPII)with 50 $mg.kg^{-1}$ of **Seenthil Sarkkarai**,group III animals (GPIII) with 100 $mg.kg^{-1}$ of **Seenthil**

Sarkkarai, group IV animals (GPIV) with 200 mg.kg^{-1} of **Seenthil Sarkkarai**, group V animals (GPV) with 400 mg.kg^{-1} **Seenthil Sarkkarai**. The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV, and V. The statistical analysis was carried out using one way ANOVA method, where **P<0.01 *P<0.05.

Effect of Seendhil Sarkkarai on kidney,heart, liver and brain in rats.

The effects of **Seendhil Sarkkarai** on kidney, heart, liver and brain of the rats were observed. From the study it was clear that, significant (p<0.01) changes in the weights of various organs of the animals occurred with higher doses of the extract (400 mg.kg^{-1}bwt), but macroscopic examinations did not show any changes in colour of the organs of the treated animals compared with the control. The results are shown in Table.3.

Treatment	Heart (gms)	Kidney (gms)	Liver (gms)	Brain (gms)
Control	0.34 ± 0.04	0.72± 0.03	3.32± 0.14	0.72± 0.05
Seendhil Sarkkarai@ 50 mg.kg^{-1}	0.36± 0.05	0.82± 0.05	3.42± 0.19	0.70± 0.03
Seendhil Sarkkarai@ 100 mg.kg^{-1}	0.39± 0.06	0.82± 0.04	3.44±0.21	0.68± 0.08
Seendhil Sarkkarai@ 200 mg.kg^{-1}	0.34± 0.03	0.75± 0.02	3.36± 0.22	0.76± 0.09
SeendhilSarkkarai@ 400 mg.kg^{-1}	0.37± 0.05	0.74± 0.02	3.38± 0.15	0.75± 0.12

Table.3

The effects of **Seenthil Sarkkarai** on kidney, heart, liver and brain of the rats. A study on the effects of **Seenthil Sarkkarai** on kidney, heart, liver and brain of the rats was tested. where, group I animals (GPI) treated with normal saline (5 ml.kg^{-1}), group II animals (GPII) with 50 mg.kg^{-1} of **Seenthil Sarkkarai**, group III animals (GPIII) with 100 mg.kg^{-1} of **Seenthil Sarkkarai**, group IV animals (GPIV) with 200 mg.kg^{-1} of **Seenthil Sarkkarai**, group V animals (GPV) with 400 mg.kg^{-1} **Seenthil Sarkkarai**. The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other

groups such as II, III, IV, and V. The statistical analysis was carried out using one way ANOVA method, where **P<0.01.

Effect of Seendhil Sarkkarai on biochemical profiles of rats

The effect of **Seendhil Sarkkarai** on various biochemical parameters of the experimental animal 'rats' were tested. From the study it was evident that, there was significant decrease ($p<0.05$) in the plasma glucose level in treated rats especially at higher dose (400 $mg.kg^{-1}$) compared with control rats. The control rats were administered only with 5 ml of normal saline. Significant decrease ($p<0.05$) in the plasma total cholesterol (TC), triglyceride (TG) and LDL-cholesterol levels were observed. But a significant increase ($p<0.05$) in HDL-cholesterol levels were observed in all the treated animals compared with the control animals. AST, ALT and ALP levels were also normal in the **Seendhil Sarkkarai** treated animals. From the results of biochemical study there was no evidence of severe toxicity associated with the administration of higher concentration of **Seenthil Sarkkarai**. The results are shown in Table.4.

Treatment	Glucose ($mg.dl^{-1}$)	Cholesterol ($mg.dl^{-1}$)	Triglyceride ($mg.dl^{-1}$)	HDL ($mg.dl^{-1}$)	LDL ($mg.dl^{-1}$)
Control	99.42±1.74	34.05± 0.62	33.25±1.43	143.45±3.15	90.30±1.85
Seendhil Sarkkarai@ 50 $mg.kg^{-1}$	97.50±1.62	30.30± 0.36*	16.36± 0.85*	181.40±3.65*	75.75±1.38
Seenthil Sarkkarai@ 100 $mg.kg^{-1}$	95.44±1.52	28.65± 0.30*	18.32± 0.90*	170.30±3.40*	74.54±1.30
Seendhil Sarkkarai@ 200 $mg.kg^{-1}$	94.30±1.35**	29.20± 0.38	20.40± 0.92*	189.34±3.70*	51.52±1.18
Seendhil Sarkkarai@ 400 $mg.kg^{-1}$	97.28±1.43**	35.45± 0.48	23.30±1.15*	187.24±3.66*	50.30±1.05

Table.4

The effect of **Seendhil Sarkkarai** on biochemical parameters such as glucose, cholesterol, triglyceride, HDL and LDL. A study on the effect of **Seenthil Sarkkarai** on biochemical parameters such as glucose, cholesterol, triglyceride, HDL and LDL in rats was tested. Where, group I animals (GPI) treated with normal saline (5 $ml.kg^{-1}$), group II

animals (GPII) with 50 mg.kg^{-1} of **Seenthil Sarkkarai**, group III animals (GPIII) with 100 mg.kg^{-1} of **Seenthil Sarkkarai**, group IV animals (GPIV) with 200 mg.kg^{-1} of, group V animals (GPV) with 400 mg.kg^{-1} **Seenthil Sarkkarai**. The values are expressed as mean ±S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV, and V. The statistical analysis was carried out using one way ANOVA method, where **P<0.01 *P<0.05

Treatment	AST (IU.l^{-1})	ALT (IU.l^{-1})	ALP (IU.l^{-1})	TP (g.l^{-1})	ALBUMIN (g.l^{-1})
Control	330.3±11.60	75.4± 3.42	255.35± 8.60	73.36± 3.31	43.30±2.45
Seenthil Sarkkarai@ 50 mg.kg^{-1}	320.4±10.52**	73.3±2.90**	267.15±8.75**	73.30±3.20	40.24±2.30
Seenthil Sarkkarai@ 100 mg.kg^{-1}	319.5±10.60**	70.3±2.92**	268.38±8.30**	83.12±3.80	41.30±2.45
Seendhil Sarkkarai@ 200 mg.kg^{-1}	318.5±9.90	67.3± 2.38	268.20±8.36	74.35± 3.65	42.28±2.46
Seendhil Sarkkarai@ 400 mg.kg^{-1}	320.4±9.94	67.6±2.45	268.42±8.44	75.30± 3.75	42.64±2.50

Table.5

The effects of **Seendhil Sarkkarai** on biochemical parameters such as AST, ALT, ALP, TP and Albumin in rats. A study on the effects of **Seendhil Sarkkarai** on biochemical parameters such as AST, ALT, ALP, TP and Albumin rats was tested. where, group I animals (GPI) were treated with normal saline (5ml.kg^{-1}), group II animals (GPII) with 50 mg.kg^{-1} of HAEBD group III animals (GPIII) with 100 mg.kg^{-1} of **Seenthil Sarkkarai**, group IV animals (GPIV) with 200 mg.kg^{-1} of **Seenthil Sarkkarai**, and group V animals (GPV) with 400 mg.kg^{-1} **Seendhil Sarkkarai** The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV, and V. The statistical analysis was carried out using one way ANOVA method, where **P<0.01 *P<0.05.

Effect of Seendhil Sarkkaraion haematological parameters in rats

The effects of **Seenthil Sarkkarai** were observed for its effect on haematological parameters on the experimental rats. From the study it was evident that, a significant increase (p<0.01) were observed in the haemoglobin contents and RBC count in the group treated with 200 mg.kg^{-1} body weight of **Seenthil Sarkkarai** and a significant

decrease of the parameters occurred in the group treated with 400 mg.kg^{-1} b.w.t compared with the control. There was no significant change in the calcium level in all the treated animals compared to the control.

Treatment	Haemoglobin (mg.dl^{-1})	RBC (10^6 /mm^3)	WBC (10^6 /mm^3)	Calcium (mg.dl^{-1})
Control	13.53±1.28	9.27± 0.93	11.54± 0.90	9.43 ±0.60
Seendhil Sarkkarai@ 50 mg.kg^{-1}	14.37±1.35*	9.35±1.05*	9.33± 0.82*	9.25 ±0.38
Seendhil Sarkkarai@ 100 mg.kg^{-1}	14.22±1.84*	9.48±1.20*	8.32± 0.28*	9.27 ±0.45
Seenthil Sarkkarai@ 200 mg.kg^{-1}	13.25±1.25*	8.37± 0.85*	11.56± 0.83*	9.55 ±0.56
Seenthil Sarkkarai@ 400 mg.kg^{-1}	13.21±1.23*	8.46± 0.92*	10.83±0.75*	9.64 ±0.64

Table.6

The effect of **Seendhil Sarkkarai** on haematological parameters such as HB, Calcium, RBC and WBC in rats. A study on the effect of **Seendhil Sarkkarai** on haematological parameters such as Hb, RBC, WBC, and Calcium in rats was tested. where, group I animals (GPI) treated with normal saline (5 ml.kg^1), group II animals (GPII) with 50 mg.kg^{-1} of **Seenthil Sarkkarai**, group III animals (GPIII) with 100 mg.kg^{-1} of **Seenthil Sarkkarai**, group IV animals (GPIV) with 200 mg.kg^{-1} of **Seenthil Sarkkarai**, and group V animals (GPV) with 400 mg.kg^{-1} **Seenthil Sarkkarai**. The values are expressed as mean ± S.E.M. n=6. The results of group I were compared with other groups such as II, III, IV and V. The statistical analysis was carried out using one way ANOVA method, where *P<0.05.

Discussion

The evaluation of sub-chronic and chronic dosing in experimental animals may be more relevant in determining the overall toxicity of the plant preparation. The highest overall concordance of toxicity in animals in comparison with humans is with hematological, gastrointestinal, and cardiovascular adverse effects whiles certain adverse effects in humans, especially hypersensitivity and idiosyncratic reactions, are poorly correlated with toxicity observed in animals (Olson, *et al*., 2000).(7)

In the present study, where the acute toxicity study of **Seendhil Sarkkarai** was carried out as per OECD-423 guidelines,no mortality was observed in both the animals of

control group as well as animals treated with a maximum dose of 2000 $mg.kg^{-1}$. Hence, $1/10^{th}$ of 2000 $mg.kg^{-1}$ i.e. 200 $mg.kg^{-1}$ of dose was selected as a minimum dose for sub-acutetoxicity study (Abu TahaNael, *et al.,* 2008).(8)

The results of sub-acute toxicity study shows that there was no significant change in animal behaviour due to the absence of toxicity. The animals treated with **Seendhil Sarkkarai** showed normal growth pattern and body weight compared with control rats treated with normal saline. So the changes in body weight can be used as an indicator of adverse effects of drugs and chemicals (Tofovic and Jackson, 1999; Raza, *et al*., 2002; Teo, 2002).(9,10,11)

The changes in enzymes like ALP, AST and ALT levels show liver impairment, due to toxicity (Hayes, 1989).(12) Serum cholesterol and proteins mainly regulated via synthesis in the liver and increase or decrease in serum concentrations of constituents suggest liver toxicity. The results of the present study were assessed after 28 days of administration of **Seenthil Sarkkarai**, and it was found that **Seendhil Sarkkarai** at all concentrations do not produce liver damage.

There was a slight decrease in plasma glucose level, when higher doses of **Seendhil Sarkkarai** (400 $mg.kg^{-1}$) were administered in the treated rats..

Analysis of blood parameters is likely to risk evaluation as the change in hematological system has a higher predictive value for human toxicity, when data are translated from animal studies (Olson, *et al*., 2000).(7) After 28 days of treatment, there were no significant changes in the haematological parameters between control and treated groups. No significant changes in the levels of WBC, RBC were observed between control and test groups following repeated administration of **Seenthil Sarkkarai**. Interestingly, significant increase in the levels of hemoglobin was found in treatment with **Seendhil Sarkkarai** with a higher dose of 400 $mg.kg^{-1}$. The possible reason could be that one of the constituents **Seendhil Sarkkarai** may increase absorption of iron.

The overall results suggest that **Seendhil Sarkkarai**are nontoxic to the haaematopoietic and leucopoietic system. The haematopoietic and leucopoietic systems are the most sensitive targets for toxic compounds and an important index of physiological and pathological status in man and animal (Adeneye, *et al.,* 2006).(13) Therefore, it is possible to assume that the **Seenthil Sarkkarai** is non haematotoxic.

ANNEXURE- IV (A)

MICROBIOLOGICAL EXAMINATION OF SEENTHIL SAKKARAI

Evaluation of Total Aerobic Bacterial Count

1.1.Preparation of Sample for Experimental Work

Weighed 10 gm of the homogenized drug sample aseptically and dissolved in 10 ml of sterile water and made up to 100 ml with the sterile water. The insoluble drug product was suspended in 100 ml of buffered sodium chloride-peptone solution (pH 7.0).

1.2.Serial dilution of Sample

A serial dilution is the dilution of a sample, in 10-fold dilutions. From the sample, 1 ml of the sample was added to 9 ml of sterile distilled water and mixed it well. This dilution was denoted as 10^{-1} dilution. From this dilution, one ml was taken from that mixture is added to 9 ml, and designated as 10^{-2} dilution. The same procedure was repeated up to 10^{-4}.

1.3. Isolation of Total Viable Aerobic Microbial Count

1.3.1. Isolation of Bacteria by Plate Count Method

In this test, the bacteria in sample were made to grow as colonies, by inoculating a known volume of sample into a solidifiable nutrient medium (Casein Soybean Digest agar or Nutrient agar medium) in petridish. The agar plate was prepared by mixing growth medium with agar and then sterilized by autoclaving. Once the agar was cooled to 45^{o}C, approximately 15 to 20 ml of medium was poured into a sterile Petri dish under aseptic condition and left to solidify for 15 minutes. After solidification, each plate was smear with 0.1 ml of sample from the dilution of 10^{-1} and 10^{-2}. After inoculations, all the plates were incubated at 37^{o}C for 24 hours. After incubation, the bacterial colonies were developed as visible to the naked eye and the number of colonies on a plate was counted using Quebec Colony Counter. Plates with an average of from 30 to 300 colonies of the target bacterium were selected for colony count. Because of the statistical problems, plates with lower than 30 colonies greater than 300 colonies were rejected

1.3.1.1. Composition of Nutrient Agar Media

Peptone	: 5.0 gm
Sodium chloride	: 5.0 gm

Beef extract	: 1.5 gm
Yeast extract	: 1.5 gm
Agar	: 15.0 gm
Distilled water	: 1000 ml
pH (at 25℃)	: 7.4±0.2

1.3.2. Isolation of Fungi

From each of the above prepared samples, 0.1 ml of sample was transferred to Sabouraud Dextrose agar (SDA) prepared with Chloramphenicol. The plates were then incubated for 5 days at room temperature (20 to 25℃). After incubation, the fungal colonies were observed and calculated.

1.3.2.1. Composition of SDA

Dextrose	; 40 gm
Peptone	: 10 gm
Agar	: 15 gm
Distilled water	: 1000 ml

1.4. Evaluation of Antimicrobial Activity of Drug

Antimicrobial activity was performed by agar well diffusion method on agar.

1.4.1 Preparation of drug extracts solutions for the experiment

The dried drugs were weighed and dissolved in sterile distilled water to prepare appropriate dilution to get required concentrations of about 10, 20 and 30µg/ml. They were kept under refrigerated condition unless they were used for the experiment.

1.4.2. Procedure for the Agar Well Diffusion Test

The antibacterial screening of the drugs were carried out by determining the zone of inhibition using agar well diffusion method. All the drug extracts were tested against four pathogenic bacterial strains of gram positive and gram negative organism by agar well diffusion method.

1.4.3. Bacterial Inoculums Preparation

Inoculums of *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Proteus vulgaris,* and *Bacillus substilis* were prepared in nutrient broth medium and kept for incubation at 37°C for 8 hrs.

1.4.4. Agar well-diffusion method

This method was followed to determine the antimicrobial activity. Muller-Hinton Agar media plates were swabbed (sterile cotton swabs) with 8 hour old - broth culture of respective bacteria. After inoculation, wells with the size of 10 mm diameter and about 2 cm a part were made in each of these plates using sterile cork borer. Stock solution of each drug extract was prepared at a concentration of 1 mg/ml in water. About 100 µl of different concentrations of drug solvent extracts were added into the wells and allowed to diffuse at room temperature for 2 hrs. The plates were incubated at 37°C for 24 hrs. After incubation, the diameter of the inhibition zone (mm) was measured and the activity index was also calculated.

1.4.4.1. Composition of Muller Hinton Agar Media

Beef Extract	: 02.00 gm
Acid Hydrolysate of Casein	: 17.50 gm
Starch	: 01.50 gm
Agar	: 17.00 gm

1.5. Evaluation of Specified Microorganisms

1.5.1. Isolation & Identification of *Escherichia coli*

One ml of the prepared sample was added in a sterile screw-capped container containing 50 ml of nutrient broth and mixed well. Then, it was allowed to stand for 1 hour and mixed well again. After one hour, the screw caps of the bottle was loosened and incubated at 37º for 18 to 24 hours.

1.5.2. Primary Test

From the above prepared enrichment culture, 1.0 ml was taken and transferred aseptically into a tube containing 5 ml of Mac- Conkey broth. Inoculated tubes were incubated in a water-bath at 36º to 38º for 48 hours.

1.5.3. Secondary Test

From the primary test, 1.0 ml of the enrichment culture was taken and transferred aseptically in to 5 ml of peptone water. It was then incubated in a water-bath at 43.5º to 44.5º C for 24 hours and observed the tubes for acid and gas. Then, the culture was subjected to biochemical tests of imvic and the results were observed and correlated.

1.5.4. Alternative test

It was done by a loop full of enriched culture in the primary test was streaked on a sterile Mac-Conkey agar medium. Then, the plates were inverted and incubated at 37 º C for 24 hours. After incubation, the pink or brick red color colonies were examined and transfer them individually into the surface of Eosin Methylene Blue agar medium (EMB), on Petri dishes. Inoculated plates were inverted and incubated at 37 º C for 24 hours. After incubation, the colonies on medium were checked for their color appearance like green metallic sheen under reflected light. The colonies were subjected to confirmation by further suitable cultural and biochemical tests.

1.5.5. Components of Eosin Methylene Blue Agar Media

Pancreatic digest of gelatin	: 10.0 g
Dibasic potassium phosphate	: 2.0 g
Lactose	: 10.0 g
Eosin Y	: 400 mg
Methylene blue	: 65 mg
Agar	: 15.0 g
Distilled water	: 1000 ml

1.5.2. Isolation & Identification of *Salmonella* sp.

One ml of the prepared sample was added in a sterile screw-capped container containing 100 ml of nutrient broth and mixed well. Then, it was allowed to stand for 1 hour and mixed well again. After one hour, the screw caps of the bottle was loosened and incubated at 37º for 18 to 24 hours.

1.5.2.1. Primary Test

From the above prepared enrichment culture, 1.0 ml was taken and transferred aseptically into a tube containing 10 ml of Selenite F broth. Inoculated tubes were incubated in a water-bath at 36º to 38º for 48 hours. After incubation, the culture was subcultured on two of the agar media namely Bismuth sulphate agar and Deoxy cholate citrate agar and incubated the plates at 36º to 38º for 18 to 24 hours. After incubation, colonies were observed on the medium and confirmed the genus *Salmonella* based on guidelines.

1.5.2.2. Secondary test

The suspected colonies of the primary test were subcultured on the slant of triple sugar-iron agar in test tube and in urea broth. Both media were incubated at 37ºC for 24 hours. After incubation, the results were observed according to the development of color change and acid / gas in media. The presence of Salmonella was confirmed by agglutination tests.

1.5.2.3. Composition of *Salmonella Shigella* Agar Media

Beef Extract	: 5.0 gm
Enzymatic Digest of Casein	: 2.5 g
Enzymatic Digest of Animal Tissue	: 2.5 gm
Lactose	: 10 gm
Bile salts	: 8.5 gm
Sodium Citrate	: 8.5 gm
Ferric Citrate	: 1.0 gm

Brilliant Green	: 0.00033 gm
Neutral Red	: 0.025
Agar	: 13.5 gm
Distilled water	: 1000 ml

1.5.3. Isolation and Identification of *Pseudomonas aeruginosa*

From the above prepared enrichment culture, 1.0 ml was taken and transferred aseptically into 100 ml of fluid soyabean-casein digest medium and mixed well. The inoculated tubes were incubated at 37º C for 24 hours. After incubation, the growth of bacteria was checked. From this, a loop full of culture was streaked on the surface of Cetrimide agar medium and Pseudomonas Isolation Agar medium and incubated at incubated at 37º C for 24 hours. After incubation, the colonies from the agar surface of these two media were checked for detection of fluorescein and pyocyanin.

1.5.3.1. Composition of Cetrimide Agar Media

Pancreatic digest of gelatin	: 20.0 g
Magnesium chloride	: 1.4 g
Potassium sulphate	: 10.0 g
Cetrimide	: 0.3 g
Agar	: 13.6 g
Glycerin	: 10.0 g
Distilled Water t	: 1000 ml

1.5.4. Isolation and Identification of *Staphylococcus aureus*

From the above prepared enrichment culture, a loop full of culture was taken and transferred aseptically on Mannitol salt agar and incubated at 37º C for 24 hours.. After incubation, the colonies were subjected to confirmation by hem agglutination test.

1.5.4.1. Composition of Mannitol Salt Agar Media

Pancreatic digest of gelatin : 5.0 g

Peptic digest of animal tissue : 5.0 g

Beef extract : 1.0 g

D-Mannitol : 10.0 g

Sodium chloride : 75.0 g

Agar : 15.0 g

Phenol red : 25 mg

Distilled Water : 1000 ml

Microbial Limit Tests

Table 1: Results of Microbial Contamination Test

S.No.	Test Particulars	Colony Counts (CFU/ g)	Limits Value (CFU/g)
1.	Total Viable Aerobic Bacterial Count	13×10^2	1×10^5
2.	Total Viable Fungal Count	No growth	1×10^3

Table 2: Results of Specific Pathogens Test

S.No.	Test for Specified Pathogens	Colony Counts (CFU/ g)	Limits Value (CFU/g)
1.	*Salmonella* sp.	No growth	-
2.	*Staphylococcus aureus*	No growth	-
3.	*Escherichia coli*	No growth	-
4.	*Pseudomonas aeruginosa*	No growth	-

Table 3: Antimicrobial Activities of Drug by Agar Well Diffusion Method

S.No.	Test Pathogens	Result	Zone of Inhibition (mm) at 30µl	
			Positive Control (Gentamycin)	Size of Inhibition
1.	*Escherichia coli*	Sensitive	26 mm	23 mm
2	*Proteus* sp.	Sensitive	23 mm	20 mm
3	*Staphylococcus aureus*	Sensitive	23 mm	20 mm
4	*Pseudomonas aeruginosa*	Sensitive	22 mm	21 mm
5.	*Salmonella typhi*	Sensitive	21 mm	19 mm

RESULTS AND DISCUSSION

The Results of the microbiological analysis for microbial contamination of the drug ***Seenthil Sakkarai*** was given in Table 1. The total viable aerobic bacterial counts on Nutrient agar plate was 13 x 10^2 CFU / g and the fungal count on SDA agar plates was NIL growth CFU/ g. This results were found to comply with the specification limit for total bacterial count i.e. NMT 1× 10^5 CFU/ml and total fungal count i.e. NMT 1× 10^3 CFU/ml (Protocol for testing Ayurveda, Siddha and Unani medicines).

The analytical screening of sample showed in Table 2 that the product is free from specific pathogen like *Escherichia coli, Proteus* sp., *Salmonella, Pseudomonas aeruginosa* and *Staphylococcus aureus.* Microbial contamination usually occurs because of improper drying or storage of the plant material which eventually results in degradation of the plant constituents. Microbial contamination can also render plant material toxic, either by transforming the chemicals in the plant material or through the production of toxic compounds by the microbes. Therefore, microbial quality tests should be applied to starting plant materials, intermediate and finished products where necessary. During the quality analysis, precautions must be taken to ensure that conditions do not adversely affect any microorganisms that are to be measured.

Thus, the present study proves that ***Seenthil Sakkarai*** is free from microbial contamination and also highlighted the safety of the same. The information obtained from microbial screening tests will be use full in finding out the quality of the drug. The good antibacterial activity of herbal medicines implies that the antimicrobial compounds present in herbal medicines are possibly controlling the microbial activity. Herbal medicines showed varying degrees of *in vitro* antibacterial activity against test bacteria.

Both Gram positive and Gram negative bacteria *E.coli, Klebsiella pneumoniae* and *Staphylococcus aureus, Pseudomonas aeruginosa and Salmonella typhi* were found to be sensitive when compared to the standard drug Gentamycin (Broad spectrum) (Table 3). The herbal drug ***Seenthil Sakkarai*** exhibited broad spectrum activity against bacterial pathogens at 100mg / ml concentration of the drug.

From these results, it is accomplished that this study would lead to the establishment of several important compounds that have to be used to formulate new, different and more potent antimicrobial drugs of natural origin. However, further studies

are required to screen the biologically active compounds and to evaluate the efficiency of this compound against pathogenic microorganisms associated with various human diseases.

ANNEXURE- IV (B)

PHYTO-CHEMICAL STUDY OF SEENTHIL SAKKARAI

This experimental study was taken up to qualitative analysis of Phyto-chemicals in the drug of ***Seenthil Sakkarai*** using various test and the results are exhibited in Table No. 4.

Table No 4: Incidence of various phyto-chemicals in *Seenthil Sakkarai*

S.No.	Name of Tests Conducted	Result Observed
Observation of Alkaloids		
1.	Mayer's Test	Positive
2.	Dragendroff's Test	Negative
3.	Hager's Test	Positive
Observation of Carbohydrates and Glycosides		
4.	Molisch Test	Positive
5.	Legal's Test	Negative
6.	Borntrager's Test for anthraquinones	Negative
Observation of Phytosterols		
7.	Liebermann – Burchard Test	Negative
8.	Salkowski Test	Negative
Observation of Flavanoids		
9.	Shinoda Test (Magnesium turnings & Hydrochloric acid)	Negative
10.	Fluorescence Test	Negative
Observation of Tannins		

11.	Ferric chloride test	Negative
12.	Potassium dichromate test	Positive
13.	Lead acetate test	Positive
14.	Millon's test	Positive
15.	Biuret test	Negative
16.	Ninhydrin test	Negative

S.No.	Name of Tests Conducted	Result Observed
Observation of fixed oils and fats		
17.	Spot test	Negative
18.	Saponification test	Positive
Observation of Lignin		
19.	Phloroglucinol test	Negative
Observation of Saponins		
20.	Frothing test	Negative

Note: *Positive indicates the presence of Phytochemical; Negative indicates the absence of Phytochemical*

ANNEXURE-V

BIOSTATISTICAL ANALYSIS OF AN A PROSPECTIVE OPEN LABELED RANDOMIZED CLINICAL Trial of "SEENTHIL SARKKARAI" for IYA NEERIZHIVU (CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TYPE II DIABETES MELLITUS)

Correlations

		B.FBS	B.PPBS	B.SU	A.FBS	A.PPBS	A.SU
B.FBS	Pearson Correlation	1	.853**	.541*	**.821****	.662**	-.079
	Sig. (2-tailed)		.000	.014	**.000**	.001	.740
	N	20	20	20	**20**	20	20
B.PPBS	Pearson Correlation	.853**	1	.362	.834**	**.758****	-.182
	Sig. (2-tailed)	.000		.117	.000	**.000**	.442
	N	20	20	20	20	**20**	20
B.SU	Pearson Correlation	.541*	.362	1	.423	.334	**.282**
	Sig. (2-tailed)	.014	.117		.063	.150	**.028**
	N	20	20	20	20	20	**20**
A.FBS	Pearson Correlation	**.821****	.834**	.423	1	.904**	-.181
	Sig. (2-tailed)	**.000**	.000	.063		.000	.445
	N	**20**	20	20	20	20	20
A.PPBS	Pearson Correlation	.662**	**.758****	.334	.904**	1	-.233
	Sig. (2-tailed)	.001	**.000**	.150	.000		.323
	N	20	**20**	20	20	20	20
A.SU	Pearson Correlation	-.079	-.182	**.282**	-.181	-.233	1
	Sig. (2-tailed)	.740	.442	**.028**	.445	.323	
	N	20	20	**20**	20	20	20

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Correlations

		B.FBS	B.PPBS	B.SU	A.FBS	A.PPBS	A.SU
B.FBS	Pearson Correlation	1	.822**	-.184	**.843****	.777**	.230
	Sig. (2-tailed)		.000	.438	**.000**	.000	.330
	N	20	20	20	**20**	20	20
B.PPBS	Pearson Correlation	.822**	1	-.430	.753**	**.822****	-.007
	Sig. (2-tailed)	.000		.058	.000	**.000**	.976
	N	20	20	20	20	**20**	20
B.SU	Pearson Correlation	-.184	-.430	1	-.301	-.393	**.714****
	Sig. (2-tailed)	.438	.058		.198	.087	**.000**
	N	20	20	20	20	20	**20**
A.FBS	Pearson Correlation	**.843****	.753**	-.301	1	.937**	-.037
	Sig. (2-tailed)	**.000**	.000	.198		.000	.878
	N	**20**	20	20	20	20	20
A.PPBS	Pearson Correlation	.777**	**.822****	-.393	.937**	1	-.089
	Sig. (2-tailed)	.000	**.000**	.087	.000		.708
	N	20	**20**	20	20	20	20
A.SU	Pearson Correlation	.230	-.007	**.714****	-.037	-.089	1
	Sig. (2-tailed)	.330	.976	**.000**	.878	.708	
	N	20	20	**20**	20	20	20

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		B.Hb	B.TC	B.DC.P	B.DC.L	B.DC.E	A.Hb	A.TC	A.DC.P	A.DC.L	A.DC.E
B.Hb	Pearson Correlation	1	-.122	-.403	.263	-.146	**.751****	-.347	-.113	.328	-.481*
	Sig. (2-tailed)		.608	.078	.262	.538	**.000**	.134	.637	.159	.032
	N	20	20	20	20	20	**20**	20	20	20	20
B.TC	Pearson Correlation	-.122	1	.356	-.418	.166	-.216	**.624****	.624**	-.541*	.158
	Sig. (2-tailed)	.608		.123	.067	.484	.360	**.003**	.003	.014	.505
	N	20	20	20	20	20	20	**20**	20	20	20
B.DC.P	Pearson Correlation	-.403	.356	1	-.820**	.225	-.139	.131	**.778****	-.720**	.285
	Sig. (2-tailed)	.078	.123		.000	.340	.558	.581	**.000**	.000	.223
	N	20	20	20	20	20	20	20	**20**	20	20
B.DC.L	Pearson Correlation	.263	-.418	-.820**	1	-.666**	.094	-.013	-.666**	**.636****	-.284
	Sig. (2-tailed)	.262	.067	.000		.001	.692	.957	.001	**.003**	.226
	N	20	20	20	20	20	20	20	20	**20**	20
B.DC.E	Pearson Correlation	-.146	.166	.225	-.666**	1	-.065	-.043	.155	-.282	**.331**
	Sig. (2-tailed)	.538	.484	.340	.001		.784	.858	.515	.228	**.154**
	N	20	20	20	20	20	20	20	20	20	**20**
A.Hb	Pearson Correlation	**.751****	-.216	-.139	.094	-.065	1	-.108	-.075	.116	-.120
	Sig. (2-tailed)	**.000**	.360	.558	.692	.784		.649	.753	.626	.616
	N	**20**	20	20	20	20	20	20	20	20	20
A.TC	Pearson Correlation	-.347	**.624****	.131	-.013	-.043	-.108	1	.243	-.320	.277
	Sig. (2-tailed)	.134	**.003**	.581	.957	.858	.649		.302	.168	.236
	N	20	**20**	20	20	20	20	20	20	20	20
A.DC.P	Pearson Correlation	-.113	.624**	**.778****	-.666**	.155	-.075	.243	1	-.871**	.262
	Sig. (2-tailed)	.637	.003	**.000**	.001	.515	.753	.302		.000	.265
	N	20	20	**20**	20	20	20	20	20	20	20
A.DC.L	Pearson Correlation	.328	-.541*	-.720**	**.636****	-.282	.116	-.320	-.871**	1	-.702**
	Sig. (2-tailed)	.159	.014	.000	**.003**	.228	.626	.168	.000		.001
	N	20	20	20	**20**	20	20	20	20	20	20
A.DC.E	Pearson Correlation	-.481*	.158	.285	-.284	**.331**	-.120	.277	.262	-.702**	1
	Sig. (2-tailed)	.032	.505	.223	.226	**.154**	.616	.236	.265	.001	
	N	20	20	20	20	**20**	20	20	20	20	20

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Correlations

		B.Hb	B.TC	B.DC.P	B.DC.L	B.DC.E	A.Hb	A.TC	A.DC.P	A.DC.L	A.DC.E
B.Hb	Pearson Correlation	1	.338	.573**	-.473*	-.286	**.727****	.031	.095	-.065	-.059
	Sig. (2-tailed)		.145	.008	.035	.221	**.000**	.896	.692	.784	.804
	N	20	20	20	20	20	**20**	20	20	20	20
B.TC	Pearson Correlation	.338	1	.313	-.456*	.394	-.035	**.828****	.094	-.034	.270
	Sig. (2-tailed)	.145		.180	.043	.086	.884	**.000**	.694	.886	.249
	N	20	20	20	20	20	20	**20**	20	20	20
B.DC.P	Pearson Correlation	.573**	.313	1	-.928**	-.185	.400	.004	**-.171**	.197	-.181
	Sig. (2-tailed)	.008	.180		.000	.435	.081	.988	**.041**	.405	.444
	N	20	20	20	20	20	20	20	**20**	20	20
B.DC.L	Pearson Correlation	-.473*	-.456*	-.928**	1	-.189	-.282	-.141	.198	**-.166**	.023
	Sig. (2-tailed)	.035	.043	.000		.426	.229	.553	.403	**.045**	.923
	N	20	20	20	20	20	20	20	20	**20**	20
B.DC.E	Pearson Correlation	-.286	.394	-.185	-.189	1	-.310	.396	-.022	-.127	**.446***
	Sig. (2-tailed)	.221	.086	.435	.426		.184	.084	.927	.594	**.009**
	N	20	20	20	20	20	20	20	20	20	**20**
A.Hb	Pearson Correlation	**.727****	-.035	.400	-.282	-.310	1	-.162	-.035	-.192	-.083
	Sig. (2-tailed)	**.000**	.884	.081	.229	.184		.496	.884	.417	.727
	N	**20**	20	20	20	20	20	20	20	20	20
A.TC	Pearson Correlation	.031	**.828****	.004	-.141	.396	-.162	1	.128	-.218	.429
	Sig. (2-tailed)	.896	**.000**	.988	.553	.084	.496		.591	.356	.059
	N	20	**20**	20	20	20	20	20	20	20	20
A.DC.P	Pearson Correlation	.095	.094	**-.171**	.198	-.022	-.035	.128	1	-.432	-.155
	Sig. (2-tailed)	.692	.694	**.041**	.403	.927	.884	.591		.057	.515
	N	20	20	**20**	20	20	20	20	20	20	20
A.DC.L	Pearson Correlation	-.065	-.034	.197	**-.166**	-.127	-.192	-.218	-.432	1	-.386
	Sig. (2-tailed)	.784	.886	.405	**.045**	.594	.417	.356	.057		.093
	N	20	20	20	**20**	20	20	20	20	20	20
A.DC.E	Pearson Correlation	-.059	.270	-.181	.023	**.446***	-.083	.429	-.155	-.386	1
	Sig. (2-tailed)	.804	.249	.444	.923	**.009**	.727	.059	.515	.093	
	N	20	20	20	20	**20**	20	20	20	20	20

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Correlations

		B.FVCL.M.PRE	B.FEV1L.M.PRE	B.FEV1.FVC.M.PRE	B.FEF25.M.PRE	B.PEFRL.M.PRE	A.FVCL.M.PRE	A.FEV1L.M.PRE	A.FEV1.FVC.M.PRE	A.FEF25.M.PRE	A.PEFRL.M.PRE
B.FVCL.M.PRE	Pearson Correlation	1	.675*	-.169	.627	.261	**.162**	.072	.082	.491	.226
	Sig. (2-tailed)		.032	.640	.052	.466	**.001**	.844	.821	.149	.531
	N	10	10	10	10	10	**10**	10	10	10	10
B.FEV1L.M.PRE	Pearson Correlation	.675*	1	.573	.849**	.510	.140	**.645***	.663*	.703*	.527
	Sig. (2-tailed)	.032		.083	.002	.132	.700	**.004**	.037	.023	.117
	N	10	10	10	10	10	10	**10**	10	10	10
B.FEV1.FVC.M.PRE	Pearson Correlation	-.169	.573	1	.427	.507	.217	.806**	**.787****	.344	.538
	Sig. (2-tailed)	.640	.083		.218	.135	.548	.005	**.007**	.330	.109
	N	10	10	10	10	10	10	10	**10**	10	10
B.FEF25.M.PRE	Pearson Correlation	.627	.849**	.427	1	.280	.211	.514	.470	**.790****	.204
	Sig. (2-tailed)	.052	.002	.218		.433	.558	.129	.171	**.006**	.571
	N	10	10	10	10	10	10	10	10	**10**	10
B.PEFRL.M.PRE	Pearson Correlation	.261	.510	.507	.280	1	.574	.639*	.390	.118	**.631**
	Sig. (2-tailed)	.466	.132	.135	.433		.083	.047	.265	.745	**.011**
	N	10	10	10	10	10	10	10	10	10	**10**
A.FVCL.M.PRE	Pearson Correlation	**.162**	.140	.217	.211	.574	1	.474	.156	.201	.064
	Sig. (2-tailed)	**.001**	.700	.548	.558	.083		.166	.666	.578	.861
	N	**10**	10	10	10	10	10	10	10	10	10
A.FEV1L.M.PRE	Pearson Correlation	.072	**.645***	.806**	.514	.639*	.474	1	.888**	.656*	.615
	Sig. (2-tailed)	.844	**.004**	.005	.129	.047	.166		.001	.039	.058
	N	10	**10**	10	10	10	10	10	10	10	10
A.FEV1.FVC.M.PRE	Pearson Correlation	.082	.663*	**.787****	.470	.390	.156	.888**	1	.679*	.688*
	Sig. (2-tailed)	.821	.037	**.007**	.171	.265	.666	.001		.031	.028
	N	10	10	**10**	10	10	10	10	10	10	10
A.FEF25.M.PRE	Pearson Correlation	.491	.703*	.344	**.790****	.118	.201	.656*	.679*	1	.314
	Sig. (2-tailed)	.149	.023	.330	**.006**	.745	.578	.039	.031		.376
	N	10	10	10	**10**	10	10	10	10	10	10
A.PEFRL.M.PRE	Pearson Correlation	.226	.527	.538	.204	**.631**	.064	.615	.688*	.314	1
	Sig. (2-tailed)	.531	.117	.109	.571	**.011**	.861	.058	.028	.376	
	N	10	10	10	10	**10**	10	10	10	10	10

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		B.HbA1C	B.LIP.TC	B.LIP.HDL	B.LIP.LDL	B.LIP.VLDL	B.LIP.TGL	A.HbA1C	A.LIP.TC	A.LIP.HDL	A.LIP.LDL	A.LIP.VLDL	A.LIP.TGL
	Pearson Correlation	1	.260	-.138	.102	.356	.395	**.732****	.172	.033	.186	.306	.402
B.HbA1C	Sig. (2-tailed)		.268	.562	.667	.124	.085	**.000**	.468	.889	.432	.189	.079
	N	20	20	20	20	20	20	**20**	20	20	20	20	20
	Pearson Correlation	.260	1	-.062	.718**	.159	.148	.252	**.870****	-.225	.765**	.056	.154
B.LIP.TC	Sig. (2-tailed)	.268		.795	.000	.504	.534	.284	**.000**	.341	.000	.813	.518
	N	20	20	20	20	20	20	20	**20**	20	20	20	20
	Pearson Correlation	-.138	-.062	1	-.004	-.307	-.480*	-.204	.054	**.378**	-.041	-.234	-.245
B.LIP.HDL	Sig. (2-tailed)	.562	.795		.987	.187	.032	.388	.822	**.100**	.863	.321	.298
	N	20	20	20	20	20	20	20	20	**20**	20	20	20
	Pearson Correlation	.102	.718**	-.004	1	-.277	-.216	.137	.548*	-.410	**.744****	-.297	-.198
B.LIP.LDL	Sig. (2-tailed)	.667	.000	.987		.238	.361	.565	.012	.073	**.000**	.204	.403
	N	20	20	20	20	20	20	20	20	20	**20**	20	20
	Pearson Correlation	.356	.159	-.307	-.277	1	.931**	.534*	.299	.283	-.183	**.862****	.866**
B.LIP.VLDL	Sig. (2-tailed)	.124	.504	.187	.238		.000	.015	.200	.227	.440	**.000**	.000
	N	20	20	20	20	20	20	20	20	20	20	**20**	20
	Pearson Correlation	.395	.148	-.480*	-.216	.931**	1	.579**	.273	.111	-.159	.807**	**.816****
B.LIP.TGL	Sig. (2-tailed)	.085	.534	.032	.361	.000		.007	.243	.640	.503	.000	**.000**
	N	20	20	20	20	20	20	20	20	20	20	20	**20**
	Pearson Correlation	**.732****	.252	-.204	.137	.534*	.579**	1	.295	.114	.038	.467*	.532*
A.HbA1C	Sig. (2-tailed)	**.000**	.284	.388	.565	.015	.007		.207	.631	.874	.038	.016
	N	**20**	20	20	20	20	20	20	20	20	20	20	20
	Pearson Correlation	.172	**.870****	.054	.548*	.299	.273	.295	1	-.148	.554*	.207	.292
A.LIP.TC	Sig. (2-tailed)	.468	**.000**	.822	.012	.200	.243	.207		.532	.011	.381	.212
	N	20	**20**	20	20	20	20	20	20	20	20	20	20
	Pearson Correlation	.033	-.225	**.378**	-.410	.283	.111	.114	-.148	1	-.537*	.037	.008
A.LIP.HDL	Sig. (2-tailed)	.889	.341	**.100**	.073	.227	.640	.631	.532		.015	.878	.974
	N	20	20	**20**	20	20	20	20	20	20	20	20	20
	Pearson Correlation	.186	.765**	-.041	**.744****	-.183	-.159	.038	.554*	-.537*	1	-.201	-.135
A.LIP.LDL	Sig. (2-tailed)	.432	.000	.863	**.000**	.440	.503	.874	.011	.015		.396	.571
	N	20	20	20	**20**	20	20	20	20	20	20	20	20
	Pearson Correlation	.306	.056	-.234	-.297	**.862****	.807**	.467*	.207	.037	-.201	1	.982**
A.LIP.VLDL	Sig. (2-tailed)	.189	.813	.321	.204	**.000**	.000	.038	.381	.878	.396		.000
	N	20	20	20	20	**20**	20	20	20	20	20	20	20
	Pearson Correlation	.402	.154	-.245	-.198	.866**	**.816****	.532*	.292	.008	-.135	.982**	1
A.LIP.TGL	Sig. (2-tailed)	.079	.518	.298	.403	.000	**.000**	.016	.212	.974	.571	.000	
	N	20	20	20	20	20	**20**	20	20	20	20	20	20

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Profoma

“A PROSPECTIVE OPEN LABELED RANDOMIZED CLINICAL TRIAL OF “SEENTHIL SARKKARAI” FOR IYA NEERIZHIVU

(CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TYPE II DIABETES MELLITUS**)”**

CONSENT FORM

CERTIFICATE BY INVESTIGATOR

I certify that I have disclosed all details about the study in the terms easily understood by the patient.

Date: ……. Signature of the Investigator: ……....

Name of Investigator: ……..

CONSENT BY SUBJECT

I have been informed to my satisfaction, by the attending physician, the purpose of the clinical trial, and the nature of drug treatment and follow-up including the laboratory investigations to be performed to monitor and safeguard my body functions.

I am aware of my right to opt out of the trial at any time during the course of the trial without having to give the reasons for doing so.

I, exercising my free power of choice, hereby give my consent to be included

As a subject in A Prospective Open Labeled Randomized Clinical Trial of “**SEENTHIL SARKKARAI”** for IYA NEERIZHIVU (CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TYPE II DIABETES MELLITUS)

Date: …… Name of the Subject: ……..

Signature or Thumb impression: ……

Date: …… Name of witness: …….

Signature or Thumb impression: ……..

Relationship: ……....

laeuo,TNehafFkUejhfrej,y rffiugh,fh,gGj j,widf fzlw,Ak kUjJtMaTxgGjy gbtk

Mathsh,d rhdw,jo

ehd ,ejMaTFw,jjmidjJt,guqfisAk Nehahs,fFg Gh,Ak tifa,y vLjJiujNjd vdcWj,as,ff,Nwd.

ifnahggk :

ngaH :

Njj, :

,lk :

Nehahs,a,d xgGjy

vdd,lk ,ejkUjJtMat,d fhuzjijAk›kUej,d jdikkwWk kUjJtto,Kiwiag gww,Ak njhlHeJvdJcly ,affjijfzfhz,ffTk›mjidg ghJfhffTk gadgLk kUjJtMaTf $l gh,Nrhjidfs gww,j,Ugj,ms,fFk tifa,y MaTkUjJtuhy t,sff,f $wgglIJ.

ehd ,ejkUjJtMat,dNghJfhuzk vJTk $whky vgnghOJNtzLkhdhYk ,ejMat,y,UeJvdidt,Lt,jJf nfhsSk ch,ikianjh,ej,Uff,Nwd.

ehd vdDilaRjej,ukhfNjHTnraAk ch,ikiaf nfhzL **laeuo,T(**COPD IN Type II Diabetes Mellitus**)**NehafFkUejhf**rej,y rffiu**gh,fh,gGj j,widf fzlw,Ak kUjJtMat,wFvdidclgLjjxgGjy ms,ff,Nwd.

ifnahggk :
ngaH :ngaH
Njj, :
,lk :
,lk :
Nkwghuitahsu ifnahggk :
Njj, :
,lk :

rhlr,a,d ifnahggk :
:
cwTKiw :
Njj, :

“A PROSPECTIVE OPEN LABELED RANDOMIZED CLINICAL TRIAL OF “SEENTHIL SARKKARAI” FOR IYA NEERIZHIVU

(CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TYPE II DIABETES MELLITUS**)”**

PATENT INFORMATION SHEET

- It is a chronic obstructive pulmonary disease
- This disease is not contagious.
- It is a clinical syndrome occurs due to pulmonary function disorder by exposure of tobacco smoking, exposure of dust and fume etc., in type II diabetes mellitus.
- Many herbal and mineral siddha medicines are currently practiced by the siddha practioners for managing the complications of Diabetes mellitus.
- The trial drug is prescribed only with evidence of siddha literature.
- The trial drug is prepared at the Gunapadam lab of government siddha medical college & hospital, palayamkottai, under the direct supervision of teaching faculties of Maruthuvam and Gunapadam Dept.

Details of the trial drug

Trial Medicine	:	SeenthilSarkkarai
Dosage	:	30 mg/ Kg/BW/daily two times a day
Adjuvant	:	Ghee
Duration	:	90 days

- Patients are advised to take green vegetables, protein foods, fibre foods, wheat.
- Patients must walk 30-45 minutes per day
- Patients are advised to avoid tamarind, betel chewing, tobacco, alcohol and smoking.

"A PROSPECTIVE OPEN LABELED RANDOMIZED CLINICAL TRIAL OF "SEENTHIL SARKKARAI" FOR IYA NEERIZHIVU

(CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TYPE II DIABETES MELLITUS**)"**

CASE REPORT FORM- SCREENING.

1. Centre: GSMC,Palayamkottai,Tirunelveli.

2. Name of the subject:……..

3. Sr. No. of the Subject: ……...

4. OP/ IP No:……..

5. Date of Admisión: …….

6. Date of Terminition: …….

4. Address: ……

5. Date of Birth: …… Age (in yrs): …….

6. Gender

Male		Female	

CRITERA OF INCLUSON

Yes	1	No	2

1	Age between 40 and 75 years	
2	Type 2 diabetes mellitus	
3	If yes in any of three	
	a. FBS > 126 mg/dl and ≤250mg/dl or	
	b. PPBS > 200mg/dl and ≤350mg /dl or	
	c. HbA1c > 6.4 and<12	
4	Persistent cases of COPD (as per the standard key indicators for assessment)	
5	FEV_1 between > 50% and <80% of the predicted value	
6	Willing to give blood sample for the investigations	
7	Patients who are mono therapy alone	

CRTERIA FOR EXCLUSION

Yes	1	No	2

8	Age below 40 and above 75	
9	If yes in any of three	
	a. FBS < 125 mg/dl and ≥251mg/dl or	
	b. PPBS <199mg/dl and ≥351mg /dl or	
	c. HbA1c < 6.4 and >12	
10	Type 1 diabetes mellitus	
11	FEV1 <50% and >80% of the predicted value	
12	Malignant and accelerated hypertension	
13	Pregnant woman and plan to pregnant six months	
14	Lactating mother	
15	Chronic kidney disease / Renal failure	
16	Corticosteroid therapy	
17	Chronic active hepatitis/cirrhosis/ascites	
18	Multisystem involvement	

A patient is eligible for admission

If 'Yes' to S.No.1 - 3 & 'No' to 4 - 12

……. ……...……

Date Signature of the Investigator

…….. ……..

SIGNATURE OF GUIDE SIGNATURE OF SUPERVISOR

……..

SIGNATURE OF HOD

“A PROSPECTIVE OPEN LABELED RANDOMIZED CLINICAL TRIAL OF “SEENTHIL SARKKARAI” FOR IYA NEERIZHIVU

(CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TYPE II DIABETES MELLITUS**)”**

Case report form II – History

1. Centre: GSMC,Palayamkottai,Tirunelveli.

2. Sr. No. of the subject: ……

3. Name of the subject: ……

4. Address: ……

5. Gender:

Male		Female	

6. Date of Birth: …….. Age (in yrs): ……

8. Educational status:

Illiterate	1	High school	5
Read and write	2	College	6
Primary	3	Others (specify)	7
Middle school	4	INA	8

9. Occupation

Desk work	1	Housewife	3
Field work	2	Others	4

Indicate nature of work: ……

10. Religion

Hindu	1	Christian	2	Muslim	3

11. Marital status

Married	1	Separated	4
Widowed	2	Single	5
Divorced	3		

11. Total Family members: ……

12. Income per capita per month (in Rs): ……

Chief complaint with duration (if any) in

Absent	0	Present	1

No	Chief complaint	0/1	Duration
13	Polyuria (Excessive Urine)		
14	Polyphagia (Excessive Hunger)		
15	Polydipsia (Excessive Thirst)		
16	Nocturia		
17	Dyspnoea		
18	Wheezing		
19	Chest pain		
20	Tightness of chest		
21	Cough		
22	Expectoration of sputum (thick and scanty/ mucoid/ mucopurulent/streaks with blood)		
23	Othres		

If Yes specify: ……

History of Present illness

Absent	0	Present	1

No	History of COPD symptoms	
24	Dyspnoea	
	A. Progressive (worsens over time)	
	B. Usually worse with exercise	
	C. Persistent (present every day)	
	D. Described by the patient as an "Increased effort to breathe, "heaviness," "air hunger," or "gasping."	
25	Chronic Cough	
	A. Intermittent	
	B. Unproductive	
26	Chronic sputum production	
	A. Any pattern of chronic sputum production	
27	Anorexia	
28	Weight loss	
29	Weight gain	

Treatment history

Yes	1	No	2

30	Ayurveda / Unani/ Homeopathic	
31	Modern medicine	

History of Past illness

Absent	0	Present	1

No	Past illness	0/1	Duration
32	History of diabetes Mellitus		
33	Repeated colds		
34	COPD		

Absent	0	Present	1

Family history

Parents	1	Sibling	2	Both	3

If present then specify:

No	Family history	0/1	1/2/3
35	Diabetes Mellitus		
36	COPD		

Personal history

Yes	1	No	2

36	Diet	
	Veg	
	Non-veg	
37	Constipation	
38	Sleep	
	satisfactory	
	unsatisfactory	

History of Environmental

Yes	1	No	2

39. Tobacco Smoking exposure ☐

If yes specify: (a) Quantity packs: ……

(b) Total Duration in year's: …….

40. Tobacco chewing ☐

If yes specify: (a) Quantity: …….

(b) Total Duration in years: ……..

41. Betel chewing

If yes specify: (a) Quantity: …….

(b) Total Duration in years: ……..

42. Alcohol

Occasional	1	Regular	2	Never	3

43. Exposure of risk factors

Absent	0	Present	1

Risk Factors of COPD	0/1	Duration
Occupational dusts and chemicals		
Smoke from home cooking		
Heating fuels		

Any other (specify):

……..

44. Thegi

Vata	1	Kapha	3	Vata-kapha	5	Sannipata	7
Pitta	2	Vata-pitta	4	Pitta-Kapha	6		

Physical Examination

45. Built

Lean	1	Medium	2	Heavy	3

46. Gait

Normal	1	Abnormal	2

47. Height (cm): …….

48. Weight (kg): …….

49. BMI {weight (kg)/Height $(m)^2$}…….

50. Pulse (per min): ……

51. Blood Pressure (in sitting position)

Systolic (mm Hg) : ……...

Diastolic (mm Hg): ……

52. Body temperature (^{o} F): ……..

53. Respiration rate (per min): ……..

Present	1	Absent	2

54	Cyanosis		
55	Jaundice		
56	Heating fuels		
57	Clubbing nails		
58	Oedema		
59	Pallor		
60	Jugular venous pulsation		
61	Lymphadenopathy		
	If present specify ,	General	
		Local	
	Area ……		

SYSTEMC EXAMINATION

Normal	1	Abnormal	2

62. Respiratory system

Shape of the chest …….

Auscultation

Present	1	Absent	2

Expiratory / inspiratory wheezes	
Inspiratory crackles	

Reduced breath sounds	

2. Cardio Vascular System ☐

If abnormal, details: ……

3.Central Nervous System ☐

If abnormal, details: ……

4. Uro-Genital system ☐

If abnormal, details: ……

5. Digestive system ☐

If abnormal, details: ……

6. Locomotor System ☐

If abnormal, details: ……

7. Endocrine System ☐

If abnormal, details: ……

8. Integumentary System ☐

If abnormal, details: ……

…….

……

Date Signature of the Investigator

…….. ……

Signature of Guide Signature of Supervisor

……..

Signature of HOD

SIDDHA SYSTEM OF EXAMINATION

A. ENVAGAI THERVU: (EIGHT-FOLD EXAMINATION)

1. NAADI (PULSE PERCEPTION)

Naadi	0st Day	14th Day	28th Day	42nd Day	56th Day	70th Day	84th Day	90th Day
Vali								
Azhal								
Iyyam								
ValiAzhal								
ValiIyyam								
AzhalVali								
AzhalIyyam								
IyyaVali								
IyyaAzhal								

2. NAA (TONGUE)

Naa	0st Day	14th Day	28th Day	42nd Day	56th Day	70th Day	84th Day	90th Day
Colour								
Taste								
Coating								
Fissure								
Saliva								
Dryness								
Glossitis								
Baldness								

3. NIRAM (COMPLEXION)

Niram	0st Day	14th Day	28th Day	42nd Day	56th Day	70th Day	84th Day	90th Day
Dark								

Yellow								
Tinted								
Pale								

4. MOZHI (VOICE)

Mozhi	0^{st} Day	14^{th} Day	28^{th} Day	42^{nd} Day	56^{th} Day	70^{th} Day	84^{th} Day	90^{th} Day
Medium								
High								
Low								
Pitched								

5. VIZHI (EYES) (Lower palpebral conjunctiva)

Niram	0^{st} Day	14^{th} Day	28^{th} Day	42^{nd} Day	56^{th} Day	70^{th} Day	84^{th} Day	90^{th} Day
Dark								
Yellow								
Red								
Pale								

6. MALAM (BOWEL HABITS / STOOLS)

Malam	0^{st} Day	14^{th} Day	28^{th} Day	42^{nd} Day	56^{th} Day	70^{th} Day	84^{th} Day	90^{th} Day
Colour								
Consistency								
Stool bulk								
Constipation								
Diarrhea								

7. URINE EXAMINATION

NEER KURI	0^{st} Day	14^{th} Day	28^{th} Day	42^{nd} Day	56^{th} Day	70^{th} Day	84^{th} Day	90^{th} Day
Niram(Colour)								

Manam(Odour)								
Nurai(Froth)								
Edai(Sp.gravity)								
Enjal(Deposits)								

NEI KURI	0st Day	14th Day	28th Day	42nd Day	56th Day	70th Day	84th Day	90th Day
Serpentine fashion								
Annular/Ringed fashion								
Pearl beaded fashion								
Mixed fashion								
Other fashion								

8. SPARISAM (PALPATORY PERCEPTION)

Sparisam	0st Day	14th Day	28th Day	42nd Day	56th Day	70th Day	84th Day	90th Day
Warmth								
Cold								
Sweat								

B. THEGI (TYPE OF BODY CONSTITUTION)

Vatham predominant	1
Kabam predominant	2
Pitham predominant	3
Thondhaudal	4

C. NILAM (LAND WHERE PATIENT LIVED MOST)

Kurinji (Hilly terrain)	1
Mullai (Forest range)	2

Marutham (Plains)	3
Neithal (Coastal belt)	4
Palai (Arid regions)	5

D. KAALAM

Kaarkalam	1	Pinpanikalam	4
Koothirkalam	2	Ilavenil	5
Munpanikalam	3	Muthuvenil	6

E. GUNAM

Sathuvam	1
Rasatham	2
Thamasam	3

F. IMPORIGAL (SENSORY ORGANS)

	0^{st} Day	14^{th} Day	28^{th} Day	42^{nd} Day	56^{th} Day	70^{th} Day	84^{th} Day	90^{th} Day
Mei (Skin)								
Vai (Buccal Cavity)								
Kann (Eye)								
Sevi (Ear)								
Mooku (Nose)								

G. KANMENDRIYAM (MOTOR FUNCTIONS)

	0st Day	14th Day	28th Day	42nd Day	56th Day	70th Day	84th Day	90th Day
Kai (Upperlimb)								
Kaal (lowerlimbs)								
Vai (buccalcavity)								
Eruvaai (excretory organs)								
Karuvaai (reproductive organs)								

H. KOSANGAL(Sheath)

	0st Day	14th Day	28th Day	42nd Day	56th Day	70th Day	84th Day	90th Day
Annamaya Kosam								
Pranamaya Kosam								
Manomaya Kosam								
Vignanamaya Kosam								
Ananthamaya Kosam								

I. MUKKUTRAM (AFFECTION OF THREE HUMORS)

A) VATHAM

	0st Day	14th Day	28th Day	42nd Day	56th Day	70th Day	84th Day	90th Day
Praanan								
Abaanan								
Viyaanan								
Udhaanan								
Samanan								
Naagan								
Koorman								
Kirukaran								
Devathathan								
Dhananjeyan								

B) PITHAM

	0st Day	14th Day	28th Day	42nd Day	56th Day	70th Day	84th Day	90th Day
Analapitham								
Ranjagam								
Saathagam								
Praasagam								
Aalosagam								

C) KAPHAM

	0st Day	14th Day	28th Day	42nd Day	56th Day	70th Day	84th Day	90th Day
Avalambagam								
Kilethagam								
Pothagam								
Tharpagam								
Santhigam								

J. SEVEN DHATHUS (7 SOMATIC COMPONENTS)

	0st Day	14th Day	28th Day	42nd Day	56th Day	70th Day	84th Day	90th Day
Saaram(Chyme)								
Senneer(Blood)								
Oon(Muscle)								
Kozhuppu(Fat)								
Enbu(Bones)								
Moolai (Bone Marrow)								
Sukkilam/Suronitham (Genital discharges)								

COLOUR		**TASTE**									
Dark	1	Sweet	1	Present	1	Normal	1	Solid	1	Normal	1
Yellow	2	Bitter	2	Absent	2	Increased	2	Watery	2	Increased	2
Red	3	Sour	3			Decreased	3	Semisolid	3	Reduced	3
Pale	4	None	4								
Tinted	5	Pungent	5								

……. ……
Date Signature of the Investigator

…….. ……
Signature of Guide Signature of Supervisor

……..
Signature of HOD

"A PROSPECTIVE OPEN LABELED NON RANDOMIZED CLINICAL TRIAL OF "SEENTHIL SARKKARAI" FOR IYA NEERIZHIVU

(CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TYPE II DIABETES MELLITUS**)"**

1. SYSTEMIC EXAMINATION

Absent	1	Present	2

	0^{st} Day	14^{th} Day	28^{th} Day	42^{nd} Day	56^{th} Day	70^{th} Day	84^{th} Day	90^{th} Day
RS								
CVS								
GIT								
CNS								
LOCOMOTOR SYSTEM								
UROGENITAL SYSTEM								
ENDOCRINE SYSTEM								

2. CLINICAL SYMPTOMS

Yes	1	No	2

	0^{st} Day	14^{th} Day	28^{th} Day	42^{nd} Day	56^{th} Day	70^{th} Day	84^{th} Day	90^{th} Day
Polyuria								
Polydipsia								
Polyphagia								
Nocturia								
Pain in the limbs								
Pain &burning sensation in the both								

sole								
Parasthesia in the feet								
Vulvo- vaginitis								
Balanitis								
Asymptomatic								

3. GENERAL EXAMINATION

	0^{st} Day	14^{th} Day	28^{th} Day	42^{nd} Day	56^{th} Day	70^{th} Day	84^{th} Day	90^{th} Day
Height (cms)								
Weight (kg)								
BMI								
Waist circumference								
Hip circumference								
Temperature (F^0)								
Pulse rate (per min)								
Heart rate (per min)								
Respiratory rate(per min)								
Blood pressure (mm/Hg)								
Anaemia								
Jaundice								
Cyanosis								
Lymphade-nopathy								
Pedal edema								
Clubbing								
Jugular vein pulsation								

Grade of Dyspnoea

Dyspnea scale Score	0^{st} Day	14^{th} Day	28^{th} Day	42^{nd} Day	56^{th} Day	70^{th} Day	84^{th} Day	90^{th} Day
Grade 0								

Grade 1								
Grade 2								
Grade 3								
Grade 4								

MMRC (Modified Medical Research Council) Dyspnea Scale Score

Equivalent to point value for highest level question to which a respondent answers "Yes."	
Dyspnea Query	**Score**
Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?	0
Do you have to walk slower than people of your age on level ground because of shortness of breath?	1
Do you ever have to stop for breath when walking at your own pace on level ground?	2
Do you ever have to stop for breath when walking about 100 yards (or after a few minutes) on level ground?	3
Are you too short of breath to leave the house or short of breath on dressing or undressing?	4

……. ……
Date Signature of the Investigator

…….. ……
Signature of Guide Signature of Supervisor

……..
Signature of HOD

"A PROSPECTIVE OPEN LABELED NON RANDOMIZED CLINICAL TRIAL OF "SEENTHIL SARKKARAI" FOR IYA NEERIZHIVU

(CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TYPE II DIABETES MELLITUS**)"**

DRUG COMPLIANCE FORM.

1. Centre: ……

2. Name of the subject: ……

3. Sr. No. of the Subject: ……

4. Address: ……

5. Date of Birth: …… Age (in yrs): ……

6. Code No. (of clinical trial): ……

7. Bed No: ……

8. Gender

Male	1
Female	2

9. Name of the Drug:

Drugs issued date:

Drugs returned date:

S.No	Date	Drug Taken Time	
		Morning/Time	Night/Time
Day 01			
Day 02			
Day 03			
Day 04			
Day 05			
Day 06			
Day 07			
Day 08			
Day 09			

Day 10			
Day 11			
Day12			
Day13			
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Day88			
Day 89			
Day 90			

…….
Date

……
Signature of the Investigator

……..
Signature of Guide

……
Signature of Supervisor

……..
Signature of HOD

"A PROSPECTIVE OPEN LABELED NON RANDOMIZED CLINICAL TRIAL OF "SEENTHIL SARKKARAI" FOR IYA NEERIZHIVU

(CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TYPE II DIABETES MELLITUS**)"**

LABORATORY PARAMETERS-CHART

1. Centre: ……

2. Name of the subject: ……

3. Sr. No. of the Subject: ……

4. Address: ……

5. Date of Birth: …… Age (in yrs): ……

6. Code No. (of clinical trial): ……

7. Bed No: …….

8. Gender

Male	1
Female	2

LAB INVESTIGATION CHART

Blood Investigation		**Normal Values**	**BeforeTMT (WithDate)**	**In Between (WithDate)**		**After TMT (WithDate)**
Hb(gms%)		M:12-15 W:11.5-14				
T.RBC(milli/cu.mm)		M:4.0-5.5 W:3.5-4.5				
ESR (mm /hr)	1/2 hr	------				
	1 hr	M:6-12 W:7-18				
T.WBC (cells /cu.mm)		4000-10000				
Differential	Polymorphs	40-75				
	Lymphocytes	20-40				

Count (%)	Monocytes	2-10				
	Eosinophil	1-6				
	Basophil	0-1				
Platelets ;(lak/ cubic mm)		1,50000-500000				
HbA1C		LESS THAN 6%				
Blood glucose (mg/dl)	Fasting	< 100				
	PP	< 140				
	Random	< 120				
Lipid profile (mg/dl)	Serum cholesterol	150-200				
	HDL	30-63				
	LDL	< 100				
	VLDL	40				
	TGL	< 160				
RFT (mg/dl)	Blood urea	20-40				
	Serum creatinine	<1.5				
	Serum Uric acid	M:2.5-6 W: 1.5-6				
LFT (mg/dl)	Total bilirubin	0.3-1.0				
	Direct bilirubin	0.1-0.3				
	Indirect bilirubin	0.2-0.7				

Urine investigation	**Before Treatment (with Date)**	**InBetween (WithDate)**		**After Treatment (With Date)**
Albumin				
Sugar(F)				
Sugar(PP)				
Sugar(R)				

Deposits				
Bile salts				
Bile pigments				
Urobilinogen				

Pulmonary Function Test

PFT	**Before Treatment (with Date)**	**InBetween (WithDate)**	**After Treatment (With Date)**
FEV_1/FVC <0.70			
FEV_1 <80%			

……. ……
Date Signature of the Investigator

…….. ……
Signature of Guide Signature of Supervisor

……..
Signature of HOD

"A PROSPECTIVE OPEN LABELED NON RANDOMIZED CLINICAL TRIAL OF "SEENTHIL SARKKARAI" FOR IYA NEERIZHIVU

(CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TYPE II DIABETES MELLITUS**)"**

WITHDRAWAL FORM

1. Centre: ……

2. Name of the subject: ……..

3. Sr. No. of the Subject: ……

4. Address: …….

5. Date of Birth: …… Age (in yrs): ……

6. Code No. (of clinical trial): ……..

7. Gender

Male	1
Female	2

8. Date of trial commencement: ……

9. Date of withdrawal from trial: ……

Reasons for withdrawal

Yes	1	No	2

Long absence at reporting	
Irregular treatment	
Shift of locality	
Increase in severity of symptoms	
Development of severe adverse drug reactions	

……. ……
Date Signature of the Investigator

…….. ……
Signature of Guide Signature of Supervisor

……..
Signature of HOD

“A PROSPECTIVE OPEN LABELED NON RANDOMIZED CLINICAL TRIAL OF “SEENTHIL SARKKARAI” FOR IYA NEERIZHIVU

(CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TYPE II DIABETES MELLITUS)”

ADVERSE DRUG REACTION FORM

1. Centre: ……

2. Name of the subject: ……

3. Sr. No. of the Subject: ……

4. Address: ……

5. Date of Birth: …… Age (in yrs): …….

6. Code No. (of clinical trial): ……

7. Gender

Male	1
Female	2

8.Date of trial commencement: …….

9. Date of withdrawal from trial: ……

10. Description of adverse reaction: ……

……. ……

Date Signature of the Investigator

…….. ……

Signature of Guide Signature of Supervisor

……..

Signature of HOD

Bibliography

BIBILIOGRAPHY

1. Anaivari R. anandan, a compendium of siddha doctrine, Chennai -600106;dept of Indian medicine and homeopathy, 2005,first edition
2. Sanmugavelu.M, Siddha Maruthuva Noi nadal Noi mudhal nadal Thirattu-part II, Chennai-106; department of Indian Medicine and Homeopathy, 2010, 2nd edition
3. Sicree R, Shaw J, Zimmet P. Diabetes and impaired glucose tolerance in India. In: Gan D, editor. Diabetes Atlas. Belgium: International Diabetes Federation; 2006.
4. http://www.searo.who.int/EN/Section1243/Section1382/Section1386/Section1898_9438.
5. World Health Organization, Regional Office for South East Asia. Health Situation in South East Asia Region (1998-2000), Regional Office for SEAR, New Delhi. 2002
6. Kuppusamy Muthaliyar,K.N, Siddha Maruthuvam –Pothu. Chennai – 600 016. Indian Medicine – Department of Homeopathy, Indian Medicine, 2012
7. Vasudevasastri, K. Vengatrajan, S, Sarabendra Vaidya Muraikal Neerizhivu Chikitsai. Thanjavur, 2012, Saraswathy Mahal Noolagam, 4th edition
8. Ramachandran,S.P. Yugimuni Vaidya Chunthamani 800. Chennai – 600 026, Thamarai Noolagam, 2013.
9. Shanmugavelu.M. Noikalukku Siddha Parikaram-part II., Chennai – 600 016. Indian Medicine, 1993, 2nd edition
10. Srinivas,P.Diabetes Mellitus(Mathumeham)-An Ayurvedic Review International journal of Pharmacy and Pharmaceutical Sciences.2014; Vol 6,Suppl 1
11. National institute of siddha,Chennai.Siddha Treatment Guidelines for selected Diseases, New Delhi, Department of AYUSH,Ministry of Health & Family Welfare Government of India & WHO Country Office for India,2014, 1st edition
12. National institute of siddha,Chennai.Development of Standard Siddha Terminologies WHO sponsored with support of Department of AYUSH,Ministry of Health & Family Welfare Government of India, Chennai-600047,Tambaram Sanatorium,2014, 1st edition
13. Harrison's et. al Diabetes mellitus. Harrison's Principal of Internal Medicine. New Delhi, MC Grew Hill Medical,2014, Vol II, 19th edition
14. Christopher, H. Edwin, R.C. & Jhon , A.A.H. Nicholas,A.B., Davidson's Principle and Practice of Medicine. London: Churchill Livingstone. 1998, 18th edition.

15. Yugimamunivar, perunoolvathiya kaaviyam, Chennai;elakkana kalnchiyam.
16. Yugimuni vaidhya kaviyam, N.G.O Colony, Vadapalani, Chennai-26; thamarai noolagam, 2002, first edition.
17. Murugesa Mudhaliyar.K.S, Gunapadam- 1st part, Chennai-106; Dept of Indian Medicine and Homeopathy, 2013, 9th edition
18. Pathinen Siddharkal vaidya sillaraikovai (Part II); N.G.O Colony, Vadapalani, Chennai-26; thamarai noolagam, 2005, first edition.
19. Agathiyar ayulvedham -1200; N.G.O Colony, Vadapalani, Chennai-26; thamarai noolagam, 1999, first edition.
20. Kalathoor Kanthasamy Mudhaliyar; pathinensiddharkal arulisetha naadi sasthiram, Chennai-79, rathina nayakkar and sons, 2012,
21. Parveen Kumar & Michael Clark(2005), Kumar&Clark Clinical Medicine.6th ed.London.pp1101-1134
22. Subramaniyan, M.A (1983), Heritage of the Tamils – Siddha Medicine, Madras - 13. International Institute of Tamil Studies, 1st ed, pp314-350.
23. Shanmuga velan. A, Siddhar's science of longevity and Kalpa Medicineof India, Chennai-106, directorate of indian Medicine and homeopathy, 1992, 2nd edition
24. Vengatrajan .S, Dhanvanthiri Vaithiyam (part II), thanjavur, directorate of Saraswathy mahal library, 2014, 4th edition
25. Mohanraj. T, Siddha Maruthuva Noi Thoguthi –I, munchirai, kanyakumari, A.T.S.V.S. Siddha Medical college and Hospital, 2010, 1st edition.
26. Kannusami Pillai.C, Kannusamiyam-Vathiyasekaram, Chennai-79, rathina nayakkar and sons, 2012
27. Sanmugavelu.M, Siddha Maruthuva Noi nadal Noi mudhal nadal Thirattu-part I, Chennai-106; department of Indian Medicine and Homeopathy, 2014, 6th edition
28. KirtikarBasu. Indian Medicinal Plants. Elsevier publications Vol. 3. 2nd edition
29. American Diabetes Association. (2004) Nutrition principles and recommendations in diabetes (Position Statement). Diabetes Care 27(Suppl. 1), S36–S46.
30. American Diabetes Association. (2004) Physical activity/exercise and diabetes (position statement). Diabetes Care 27, S58–S62.
31. American Diabetes Association. (2004) Dyslipidemia management in adults with diabetes. Diabetes Care 27(Suppl. 1), S68–S71.
32. American Diabetes Association (2010) Position Statement; Standards of Medical Care in Diabetes - 2010. Diabetes Care; 33(Suppl-1): S11-61.

33. American Diabetes Association (2009) Workshop Report; International Expert Committee Report on the Role of the A1C Assay in the diagnosis of Diabetes. Diabetes Care; 32: 1327-34.
34. Anonymus. Sarabenthirar Vaidhiya Muraigal-Neerizhivu Chiikitchai, Thanjavur, Saraswathi Mahaal Noolagam, 1992; 3rd Edition.
35. Kannusamy pillai C. Sikitcha Rathna Deepam Ennum Vaidiya Nool,. 1991;Vol 1, 3rd edition.
36. Ramachandran S.P, Agasthiyar Vaithya Rathinachurukkam, Thamarai Noolagam. 1994;May.
37. Rogliani et al. COPD Research and Practice 1:3. 2015.
38. American Review of Respiratory Disease (Issue 1987), Cross-Section Study of Pulmonary Function in Patients with Insulin-dependent Diabetes Mellitus, Volume 135.
39. Hiroshi mori, Abnormalities of Pulmonary function in Patient with Non-Insulin Dependent Diabetes mellitus, Internal medicine, Issue 1992;Volume 31.
40. Soham Saha, Tinospora cordifolia: One plant, many roles Anc Sci Life, 31(4): 2012;Apr-Jun.
41. Vaibhav D. Aher, , Pharmacological Study of Tinospora Cordifolia As An Immunomodulator, International Journal of Current Pharmaceutical Research, Volume 2,Issue 4;2010)
42. Christopher, H. Edwin, R.C. & Jhon , A.A.H. Nicholas,A.B., Davidson's Principle and Practice of Medicine.18th ed. London:Churchill Livingston; 1998.

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For participating as ~~Resource~~ ~~Person~~ / Delegate in the Twentieth Workshop on

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*For **AYUSH Post Graduates & Researchers***

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The Tamil Nadu Dr. M.G.R. Medical University From 07th to 11th March 2016.

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GOVERNMENT SIDDHA MEDICAL COLLEGE
PALAYAMKOTTAI

SCREENING COMMITTEE

Registration No. of the Candidate:.....

DEPARTMENT OF POTHUMARUTHUVAM

This is to certify that the dissertation topic **IYA NEERIZHIVU (CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN PATIENTS WITH TYPE II DIABETES MELLITUS) with *"Seenthil Sarkkarai"*** has been approved by the screening committee.

Branch	Department	Name	Signature
1	Pothu Maruthuvam	Dr.A.Manoharan. MD(S)., Professor	
2	Gunapadam	Dr.A.Kingsly MD(S)., Associate Professor	
3	Sirappu Maruthuvam	Dr.A.S.Poongodikanthamathi MD(S)., Professor	
4	Kuzhandhai Maruthuvam	Dr.D.K.Soundararajan. MD(S)., Professor	
5	Noi Nadal	Dr.S.Victoria MD(S)., Professor	
6	Nanju Nool Maruthuvam	Dr.M.Thiruthani. MD(S)., Professor	

Remarks:

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R.No. GSMC/5676/P&D/Res/IEC/2014 **Date: 20.07.2016**

CERTIFICATE OF APPROVAL

Address of Ethical Committee	Government Siddha Medical College, Palayamkottai-627002, Tirunelveli district.
Principal Investigator	Dr.Sarangapany Uthyanan,MD(s), First year, Department of Pothu Maruthuvam, Reg. No: Not yet registered.
Supervisor	**Prof.Dr.A.Manoharan, M.D$_{(s)}$.,** Head of the Department, Department of Pothu Maruthuvam, Government Siddha Medical College and Hospital, Palayamkottai - 627002, Tirunelveli District. drmanoharan25@gmail.com
Guide	**Dr.S.Justus Antony, M.D(s).,** Lecturer Greade II, Department of Pothu Maruthuvam Government Siddha Medical College and Hospital, Palayamkottai - 627002, Tirunelveli District. Justusantony71@gmail.com
Dissertation Topic	A Prospective open labelled Randomized Clinical trial on herbal formulation of ***"Seenthil Sarkkarai"*** for the treatment of **IYA NEERIZHIVU** (CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN PATIENTS WITH TYPE II DIABETES MELLITUS)
Documents Filed	(1)Protocol (2)Data Collection Forms (3)Patient Information Sheet (4)Consent Form (5)SAE (Pharmacovigilance)
Clinical/Non Clinical Trial Protocol (Others-Specify)	Clinical Trial Protocol-yes
Informed Consent Document	Yes
Any other Document	Case Sheet/Investigation Documents
Date of IEC Approval & its Number	20.07.2016 , GSMC/3-IEC/2016-I-6/20.07.2016

We approve the trial to be conducted in its presented form.

The Institutional Ethical Committee expects to be informed about the process report to be submitted to the IEC at least annually of the study, any SAE occurring in the course of the study, any changes in the protocol and submission of final report.

Chairman
20/7/2016
(Prof. Dr. M.Logamanian Ph.D.,)

Member Secretary
20/7/16
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UNDER THE DIRECTORATE OF
INDIAN MEDICINE AND HOMEOPATHY,
GOVERNMENT OF TAMIL NADU

APPLICATION FORM TO BE SUBMITTED TO THE INSITUTITIONAL ETHICAL COMMITTEE FOR APPROVAL OF RESEARCH PROPOSALS

IEC CODE NUMBER	GSMC/3-IEC/2016-I-6/20.07.2016	DATE:	20.07.2016

Applications Accepted	Proposal Approved
20/7/16	20/7/2016
Secretary IEC	Secretary IEC
Date:	Date:

1

GOVERNMENT SIDDHA MEDICAL COLLEGE

PALAYAMKOTTAI

Certificate of Botanical Authenticity

Certified the following plant drugs used in Siddha formulation (Internal) ***"SEENTHIL SARKKARAI"*** for **IYA NEERIZHIVU** (CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TYPE II DIABETES MELLITUS) taken up for Post-Graduation Dissertation Studies by Dr.Sarangapany Uthayanan PG Scholar MD siddha, Department of Pothu Maruthuvam are correctly identified and authenticated through Visual inspection / Organoleptic Characters / Experience, Education & Training Morphology Microscopically and Taxonomical methods.

Table 1: Ingredient of Seendhil Sarkkarai

S.N	Name	Botanical Name	Family	Parts Used
1.	Seenthil	*Tinospora cordifolia.*	Menispermaceae	Stem

Station: Palayamkottai

Date: 28.12.16

28/12/16

Authorized Signature

Dr. S. SUTHA, M.Sc.,M.Ed.,Ph.D.,
Associate Professor
Dept. of Medicinal Botany
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(For IAE / CPCSEA usage)

Proposal number	:	**SARANGAPANY UTHAYANAN/321511006/ MD(S)/TNMGRMU/KMCP/IAEC/312**
Date first received	:	12.02.2017
Date received after modification (if any)	:	NA
Date received after second modification (if any)	:	NA
Approval date	:	15.02.2017
Expiry date	:	31.07.2017
Name of IAEC / CPCSEA chairperson	:	Dr. N. CHIDAMBARANATHAN

Date: 15.02.2017

15/2/17

CPCSEA NOMINEE
INSTITUTIONAL ANIMAL ETHICS COMMITTEE
K.M. COLLEGE OF PHARMACY
MADURAI-625 107

Signature 15/2/17

I. A. E. C. CHAIRMAN
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CONTINUING MEDICAL EDUCATION PROGRAMME

Conducted by

Post Graduate Department of Pothu Maruthuvam

This Certificate is awarded to Dr / ~~Mr~~ / ~~Mrs~~ SARANGAPANY UTHAYANAN .....

has participated in the CME Programme held on 13.06.2018 at Conference Hall Special Therapy Wing, Government Siddha Medical College, Palayamkottai, Tirunelveli. This Programme is focussed on

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IN COLLABORATION WITH

MINISTRY OF AYUSH Govt OF INDIA

NORTHERN PROVINCIAL COUNCIL

1ST INTERNATIONAL CONFERENCE & EXHIBITION ON SIDDHA MEDICINE -2018

23RD - 27TH AT UNIT OF SIDDHA MEDICINE
UNIVERSITY OF JAFFNA.
SRI LANKA

CERTIFICATE

THIS IS TO CERTIFY THAT Prof. / Dr. / Mr./ Ms./ ...SARANGAPANY UTHAYANAN.....PARTICIPATED IN THE PRE- CONFERENCE WORK SHOP HELD ON 23RD – 25TH FEBRUARY 2018, AT UNIT OF SIDDHA MEDICINE, UNIVERSITY OF JAFFNA, KAITHADY.

Prof . R. VIGNESWARAN
VICE CHANCELLOR
UNIVERSITY OF JAFFNA

Shri. A. NATRAJAN
CONSULATE GENERAL,
HIGH COMMISSION OF INDIA
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ANTI-HYPERGLYCEMIC EFFECT AND EFFECT OF ANTI -OXIDANT ENZYMES INVOLVED IN METABOLISM OF *SEENDHIL SARKKARAI* IN EXPERIMENTAL ANIMAL

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ABSTRACT

Background: *Seendhil* (*Tinospora cordifolia)* is widely used for medicinal purpose. *Seendhilsarkkarai*has been used traditionally as anti-hyperglycemic in Siddha System of medicine.**Objectives:** The present study was undertaken to evaluate the anti–hyperglycemic and anti-hyperlipidemic effects on anti – oxidant enzymes involved in metabolism of *seendhilsarkkarai*in Streptozotocin induced diabetic rats. **Materials and method:** Wistar strains of male albino rats weighing between 180-220gm are used for this study. Diabetes mellitus is induced in wistar rats by single intraperitoneal injection of freshly prepared solution of Streptozotocin (25mg/kg BW) in physiological saline after overnight fasting for 12hrs.The body weights of the rats in every group were recorded weekly. five groups of 6 animals in each received normal saline for normal control, glipizide at a dose of (10mg/Kg orally) for diabetic control, *SeendhilSarkkarai* at a dose of (100mg/Kg orally) and 200mg/kg for euglycemic rat for 28 days,After 28 days of treatment, body weight, blood glucose, haemoglobin, glycosylated haemoglobin, plasma insulin, total cholesterol, triglycerides, HDL-cholesterol and

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Acute Toxicity Study Of Herbal Formulation of "Avaraivithathi Chooranam" In Albino Mice

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ABSTRACT

OBJECTIVE: To evaluate the acute toxicity of herbal formulation of *Avaraivithathi chooranam* in albino mice.

METHODS: *Avaraiviththathi Chooranam* is administered by gastric intubations to the relevant group of animals orally at the dose of 50, 300, 2000 mg/kg body weight in Tween-80. The animals are then observed for 14 days and maintained with normal food. Toxic symptoms are observed for 72 hrs including behavioural changes, locomotion, convulsions and mortality.

RESULTS: There was no mortality or morbidity observed in animals through the 15-days period following single oral administration at all selected dose levels of the *Avaraiviththathi Chooranam.* The animals did not show any changes in the general appearance during the observation period. Gait and posture, reactivity to handling or sensory stimuli, grip strength was also normal.

CONCLUSIONS: No mortality was observed in both the animals of control group as well as animals treated with a maximum dose of 2000 mg/kg. These results indicate the safety of the oral administration of *Avaraivithathi Chooranam.*